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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : G01N 33/573, C12N 9/12, C07K 14/435	A1	(11) International Publication Number: WO 97/37224 (43) International Publication Date: 9 October 1997 (09.10.97)

(21) International Application Number: PCT/GB97/00898

(22) International Filing Date: 1 April 1997 (01.04.97)

(30) Priority Data:
9606765.7 30 March 1996 (30.03.96) GB
9626362.9 19 December 1996 (19.12.96) GB

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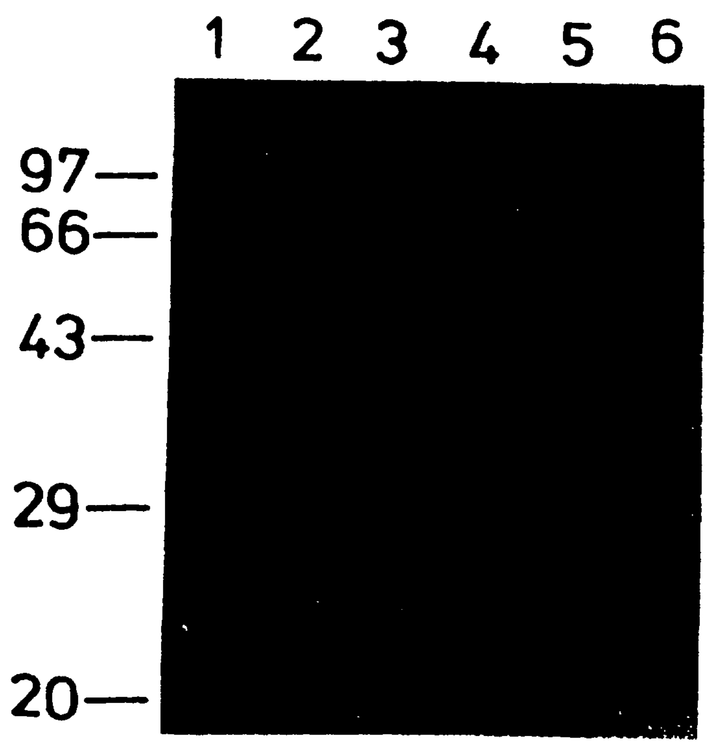
(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ARIPO patent (GH, KE, LS, MW, SD, SZ, UG), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).

Published
With international search report.
Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(54) Title: PROTEIN PHOSPHATASE-1 CATALYTIC SUBUNIT INTERACTIONS

(57) Abstract

A method of identifying a compound which modulates the interaction between a PP1c and a regulatory subunit thereof, the method comprising determining whether a compound enhances or disrupts the interaction between (a) a PP1c or a fragment, variant, derivative or fusion thereof or a fusion of a fragment, variant or derivative and (b) a regulatory subunit which is able to bind to PP1c or a PP1c-binding fragment, variant, derivative or fusion of said subunit or a fusion of said fragment, variant or derivative. A method of affecting cellular metabolism or function, the method comprising administering to a cell (a) a compound which modulates the interaction between a PP1c and a regulatory subunit thereof or (b) a compound which mimics the effect of a regulatory subunit of PP1c or (c) a peptide capable of binding a PP1c and which affects the ability of PP1c to bind to a particular target and/or affects the regulation of PP1c activity, or a functional equivalent thereof.



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PROTEIN PHOSPHATASE-1 CATALYTIC SUBUNIT INTERACTIONS

The present invention relates to peptides and protein-protein interactions and to the use of peptides, peptide analogues and compounds which modulate protein-protein interactions in the control of cellular metabolism and function.

Cellular metabolism or function is controlled by a number of regulatory agents, which are affected by extracellular factors, for example the physical condition of the cell or the binding of a messenger molecule to a receptor located on the cell surface. The extracellular factor may then initiate a cascade of secondary messenger reactions within the cell itself, leading ultimately to changes in some aspects(s) of metabolism or cell function.

It is well recognised by those skilled in the art that phosphorylation or dephosphorylation reactions often play a key role in regulating the activity of the proteins affected. Dephosphorylation reactions are catalysed by phosphatase enzymes, the activity of which may themselves be controlled by phosphorylation and/or dephosphorylation events. Whilst a substantial amount of knowledge has been accumulated regarding protein phosphatases as a group, the number and variety of these enzymes is such that detailed information concerning the mode of action of a specific phosphatase is not always available. There remains a need to further elucidate and characterise particular key enzymes.

The reversible phosphorylation of proteins regulates most aspects of cell life. About a third of all mammalian proteins are now thought to contain covalently bound phosphate and, since protein kinases and phosphatases probably account for approximately 2-3% of all human gene products (Hunter, 1995), many of these enzymes must typically phosphorylate/dephosphorylate numerous proteins *in vivo*. However, it is becoming increasingly clear that some protein kinases

and phosphatases do not find their physiological substrates by simple diffusion within cells and that they are frequently directed to particular loci in the vicinity of their substrates by interaction with targeting subunits. In this way, the actions of protein kinases and phosphatases with inherently broad specificities are restricted and their properties tailored to the needs of a particular subcellular location, organelle or process (reviewed in Hubbard and Cohen, 1993; Faux and Scott, 1996).

Protein phosphatase-1 (PP1), one of the major protein serine/threonine phosphatases of eukaryotic cells, participates in the control of a variety of cellular functions that include glycogen metabolism, muscle contraction, the exit from mitosis (reviewed in [1,2]) and the splicing of mRNA [3]. However, evidence has been accumulating that different processes are regulated by distinct forms of PP1 in which the phosphatase catalytic subunit (PP1c) is complexed to specific "targeting subunits". These proteins not only direct PP1c to particular subcellular locations, but modify its specificity in unique ways and confer regulation by extracellular agonists (reviewed in [2,3]).

Several targeting subunits have been isolated and characterised, including the G_M-subunit that targets PP1c to both the glycogen particles and sarcoplasmic reticulum of striated muscles [4,5], the G_L subunit that targets PP1c to liver glycogen [6,7], the M-complexes responsible for the association of PP1c with the myofibrils of skeletal muscle [8,9] and smooth muscle [9-12], the p53 binding protein p53BP2 [13] and nuclear proteins such as sds22 [14] and NIPP1 [15,16]. PP1c is also reported to interact with other mammalian proteins such as the retinoblastoma gene product [17], ribosomal protein L5 [18], a 110 kDa nuclear protein that has yet to be identified [15] and two cytosolic proteins, termed inhibitor-1 and inhibitor-2. Inhibitor-1, and its homologue termed dopamine and cyclic AMP-regulated phosphoprotein (DARPP), become potent PP1 inhibitors after phosphorylation by cyclic AMP-dependent protein kinase

(PKA). Inhibitor-1 is thought to inactivate PP1c released from glycogen particles when G_M is phosphorylated by PKA [19]. Inhibitor-2 is present as a complex with PP1 in the cytosol, and there is evidence that one of its roles is to act like a molecular chaperone to ensure that the PP1 catalytic centre is folded correctly prior to its delivery to a specific targeting subunit [20]. It seems likely that many other PP1-targeting subunits will be identified over the next few years as a result of the introduction of powerful new techniques such as microcystin Sepharose affinity chromatography [8] and the yeast "two hybrid system" [13].

The forms of PP1c isolated so far each contain a single PP1c-binding subunit, implying that the interaction of different targeting subunits with PP1c may be mutually exclusive. This, in turn, suggests that the binding sites for targeting subunits may overlap, and that the proportion of PP1 directed to any particular location may be determined by the amounts of each targeting subunit synthesised and their relative affinities for PP1. However, the different targeting subunits show surprisingly little similarity to one another. G_M and G_L are structurally related, yet display only 23% amino acid sequence identity over the first 286 residues of G_M, while G_L lacks the C-terminal 750 residues of G_M [7]. p53BP2 [13] and the M_{110} subunits from smooth muscle [10,11] and skeletal muscle [8] contain ankyrin repeats, but no other similarities have so far been detected between other PP1 targeting subunits.

The paradigm for the targeting subunit concept is protein phosphatase-1 (PP1), one of the major serine/threonine specific protein phosphatases of eukaryotic cells (Stralfors *et al.*, 1985). This enzyme is involved in controlling diverse cellular functions including glycogen metabolism, muscle contraction, the exit from mitosis and the splicing of RNA (Cohen, 1989; Shenolikar, 1994; Wera and Hemmings, 1995). These different processes appear to be regulated by distinct PP1 holo-enzymes in which the same catalytic subunit (PP1c) is

complexed to different targeting or regulatory subunits. The latter class of subunits act to confer *in vivo* substrate specificity not only by directing PP1c to the subcellular loci of its substrates, but also by enhancing or suppressing its activity towards different substrates. In addition, the regulatory subunits allow the activity of PP1 to be modulated by reversible protein phosphorylation and second messengers in response to extracellular stimuli.

Many regulatory subunits modulate the activity of PP1 towards its substrates. In the instance of the regulatory M_{110} subunit that targets PP1c to myosin, the region on the M_{110} subunit that enhances the dephosphorylation of myosin by PP1 has now been shown to be distinct from the region involved in targetting the PP1-M holoenzyme to myosin. These observations indicate that alterations in the substrate specificity of PP1c are likely to result from conformational changes induced by interactions with the targetting subunit and not simply as a direct result of targetting PP1c to its substrate. However, in the case of the glycogen binding subunit G_M, the dephosphorylation of glycogen phosphorylase and glycogen synthase was enhanced only under conditions when both the PP1-G_M complex and its substrates were bound to glycogen (Hubbard and Cohen, 1989) suggesting that targetting alone may be sufficient to enhance specificity.

Whilst the identity of the PP1-binding site(s) on any targeting subunit is unknown, it has now been realised that the control of the substrate specificity and activity of this key regulatory enzyme and its interactions are of therapeutic importance. Disruption of PP1-targeting subunit interactions provide a way of altering selectively the state of phosphorylation, and hence the activities, of particular PP1 substrates. We have now identified relatively small peptides from the G_M and M_{110}-subunits that interact with PP1, and which either disrupt or mimic the distinctive properties of myofibrillar and glycogen-associated forms of PP1. The binding of the G-subunit and the M-subunit of PP1 has also

been found to be mutually exclusive.

A first aspect of the invention provides a method of identifying a compound which modulates the interaction between a PP1c and a regulatory subunit thereof, the method comprising determining whether a compound enhances or disrupts the interaction between (a) a PP1c or a fragment, variant, derivative or fusion thereof or a fusion of a fragment, variant or derivative and (b) a regulatory subunit which is able to bind to PP1c or a PP1c-binding fragment, variant, derivative or fusion of said subunit or a fusion of said fragment, variant or derivative.

Conveniently, the PP1c or a fragment, variant or derivative or fusion thereof or a fusion of a fragment, variant or derivative is one that is produced using recombinant DNA technology. By "fragment, variant, derivative or fusion of PP1c" we mean any such fragment, variant, derivative or fusion that retains the ability to interact with a regulatory subunit or a suitable PP1c-binding fragment, variant, derivative or fusion of said subunit or a fusion of said fragment, variant or derivative.

By "regulatory subunit" we mean any such regulatory subunit. Further subunits are being identified all of the time. It is preferred if the regulatory subunit contains the consensus peptide sequence Arg/Lys-Val/Ile-Xaa-Phe as described below.

By "PP1c-binding fragment, variant, derivative or fusion of said subunit or a fusion of said fragment, variant or derivative" we include any such fragments, variants, derivatives and fusions which are able to bind to PP1c. Conveniently, the fragments, variants, derivatives are made using recombinant DNA technology or, in the case of peptides and peptide derivatives and analogues they may be made using peptide synthetic methods.

The enhancement or disruption of the interaction between the said PP1c or a fragment, variant, derivative or fusion thereof or a fusion of a fragment, variant or derivative and the said regulatory subunit or a fragment, variant, derivative or fusion thereof or a fusion of a fragment, variant or derivative can be measured *in vitro* using methods well known in the art of biochemistry and including any methods which can be used to assess protein-protein, protein-peptide and protein-ligand interactions.

The said interaction can also be measured within a cell, for example using the yeast two-hybrid system as is well known in the art.

It should be appreciated that before the present invention the dissociation of a PP1c-regulatory subunit has not been achieved using a small molecule such as a peptide or a peptide analogue or derivative. Thus, it is preferred if the compounds screened in the method of the first aspect of the invention are small molecules and in particular that they are not intact regulatory subunits of PP1c.

By "small molecule" we include any compounds which have a molecular weight of less than 5000, preferably less than 2000 and more preferably less than 1000. Conveniently, the compounds screened are compounds which are able to enter a cell either passively *via* the cell membrane or *via* an active uptake system.

A second aspect of the invention provides a method of identifying a compound which mimics the effect of a regulatory subunit of PP1c, the method comprising contacting said compound with PP1c and determining whether, in the presence of the compound, PP1c adopts the function of properties of a PP1c in the presence of a given regulatory subunit.

By "mimics the effect of a regulatory subunit of PP1c" we include the meaning

that the compound modifies a property of PPlc in such a way that PP1c acts, in at least one respect, like PP1c that is interacting with a regulatory subunit.

Examples of the properties of PP1c that may be modified, and examples of compounds which modify the properties of PP1c which are therefore identifiable in this method are given below.

Preferably, in the methods of the first and second aspects the said regulatory subunit of PP1c is any one of M_{110}, G_L, G_M, M-complexes, p53 BP2, sds22, NIPPI, L5, Inhibitor-1, Inhibitor-2, or DARPP.

More preferably, the regulatory subunit of PP1c is any one of M_{110}, G_L, G_M, M-complexes or p53BP2, and still more preferably the regulatory subunit of PP1c is M_{110} or G_M.

In relation to the method of the first aspect of the invention the fragment of a regulatory subunit which is able to bind to PP1c is any of the peptides [G63-T93], [G63-N75], [E2-R575], [E2-P243], [E2-D118], [H100-P350] and peptide 63-80 of G_M or functional equivalents thereof or peptides comprising said peptide sequences provided that they are not the complete G_M regulatory subunit. Preferably the peptides are not [E2-R575] or [H100-P350].

As is described in more detail in the Examples, these peptides have been shown to bind to PP1c and it is convenient, in some circumstances, for the method to be carried out such that one of these peptide is displaced from, or the binding is enhanced to, PP1c. Suitably, the peptide may be labelled in a detectable manner to facilitate the detection of the interaction with PP1c. Conveniently, the peptide is labelled radioactively or fluorescently using methods well known in the art.

Also in relation to the method of the first aspect of the invention the fragment of a regulatory subunit which is able to bind to PP1c is any of the peptides [M1-E309], [M1-F38], [M1-A150] or [L24-Y496] of M_{110} or functional equivalents thereof or peptides comprising said peptide sequences provided that they are not the complete M_{110} regulatory subunit.

As is shown in more detail in the Examples these peptides have been shown to bind to PP1c.

Also in relation to the first aspect of the invention the PP1c-binding fragment, variant or derivative of said regulatory subunit or a fusion of said fragment, variant or derivative comprises the consensus peptide sequence Arg/Lys-Val/Ile-Xaa-Phe wherein Xaa is any amino acid.

We have found that, surprisingly, many regulatory subunits that bind to PP1c contain the consensus peptide sequence Arg/Lys-Val/Ile-Xaa-Phe wherein Xaa is any amino acid, preferably a naturally occurring amino acid. Typically, the PP1c-binding fragment, variant or derivative of said regulatory subunit or a fusion of said fragment, variant or derivative is a peptide (typically 8-400 amino acid residues, preferably 8-200, more preferably 8-10 and still more preferably 8-20 amino acid residues in length which comprises the given consensus peptide sequence).

It is preferred if the PP1c-binding fragment, variant or derivative comprises, in addition to the said consensus peptide sequence, at least one basic residue in the four residues N-terminal of the consensus peptide sequence. Preferably, there are at least two basic residues in this position, more preferably at least three such residues.

It is also preferred wherein in the consensus peptide sequence Xaa is not Asp

or Glu because the negative charge is believed to interfere with binding to PP1c. Similarly, it is preferred if Xaa is not a large hydrophobic residue such as Phe, Tyr, Trp, Ile or Leu.

It is particularly preferred if the PP1c-binding fragment is a fragment of a regulatory subunit comprising the said consensus peptide sequence and therefore the peptide sequences which flank the consensus peptide sequence are the same as in the native regulatory subunit.

Preferably the PP1c-binding fragment is a fragment of any of the M_{110}, G_L, G_M, M-complexes, p53BP2, sds22, NIPPI, L5, Inhibitor-1, Inhibitor-2 or DARPP regulatory subunits comprising said consensus sequence.

Although the methods of the first and second aspects of the invention do not rely on any particular mechanism whereby the modulation or mimicking occurs, it is preferred if the compound binds to a PP1c. Alternatively, but still preferably, the compound binds to a regulatory subunit of PP1c.

A further aspect of the invention provides a compound identifiable by the method of the first or second aspects of the invention.

A further aspect of the invention provides a compound which modulates the interaction between a PP1c and a regulatory subunit thereof said compound comprising any of the peptides [G63-T93], [G63-N75], [E2-R575], [E2-P243], [E2-D118], [H100-P350] and peptide 63 to 80 of G_M or functional equivalents or said compound comprising any of the peptides [M1-E309], [M1-F38], [M1-A150] or [L24-Y496] of M_{110} or functional equivalents thereof or said compound comprising the consensus peptide sequence Arg/Lys-Val/Ile-Xaa-Phe wherein Xaa is any naturally occurring amino acid or functional equivalents thereof, provided that the said compound is not a complete regulatory subunit

of PP1c. Preferably, the peptides are not [E2-R575] or [H100-P350].

By "functional equivalent" we include the meaning that the compound, although having a different structure to the said peptides, modulates the interaction between a PP1c and a regulatory subunit thereof in substantially the same way. For example, a functional equivalent may be a peptide in which conservative substitutions have been made. By "conservative substitution" is intended combinations such as Gly, Ala; Val, Ile, Leu; Asp, Glu; Asn, Gln; Ser, Thr; Lys, Arg; and Phe, Tyr. A functional equivalent may also be a peptide with the given sequence which has been adapted to be more likely to enter a cell. For example, fatty acids or other hydrophobic moieties may be attached to the peptide.

By the term "peptide" we mean derivatives of peptides which are resistant to proteolysis, for example those in which the N or C termini are blocked, or both are blocked, and it includes molecules in which one or more of the peptide linkages are modified so that the molecule retains substantially the same molecular configuration in the linkage but the linkage is more resistant to hydrolysis than a peptide linkage.

It is particularly preferred if the compound consists of the peptides [G63-T93], [G63-N75], [E2-R575], [E2-P243], [E2-D118], [H100-P350] or peptide 63 to 80 of G_M or functional equivalents thereof or if the compound consists of the peptides [M1-E309], [M1-F38], [M1-A150] or [L24-Y496] of M_{110} or functional equivalents thereof. Preferably, the peptide is not [E2-R575] or [H100-P350].

A still further aspect of the invention provides a method of identifying a compound which modulates the interaction between a PP1c and a regulatory subunit thereof, or binds PP1c or mimics the effect of a regulatory subunit, the

method comprising selecting a compound which is capable of adopting the same or substantially the same conformation as a peptide bound to the regulatory subunit-binding site of PP1c or the same or substantially the same conformation as the portion of PP1c which binds to said peptide. Suitably, the peptide comprises the consensus peptide sequence Arg/Lys-Val/Ile-Xaa-Phe wherein Xaa is any amino acid, preferably a naturally occurring amino acid. Conveniently, the said peptide consists of residues 63 to 75 of G_M.

It is particularly preferred if the conformation of the said peptide and the conformation of the said portion of PP1c is as defined by reference to the atomic coordinates given in Table A (see also Example 2). Example 2 provides further details of the peptide - PP1c interactions.

Table A provides the atomic coordinates for the given PP1c-peptide crystal structure.

A further aspect of the invention provides a compound identifiable by the aforementioned method of the invention.

It will be appreciated that the aforementioned compounds and peptides will be useful in medicine and, accordingly, the invention includes pharmaceutical compositions of the said compounds in combination with a pharmaceutically acceptable carrier.

The formulations may conveniently be presented in unit dosage form and may be prepared by any of the methods well known in the art of pharmacy. Such methods include the step of bringing into association the active ingredient (compound of the invention) with the carrier which constitutes one or more accessory ingredients. In general the formulations are prepared by uniformly and intimately bringing into association the active ingredient with liquid carriers

or finely divided solid carriers or both, and then, if necessary, shaping the product.

Formulations in accordance with the present invention suitable for oral administration may be presented as discrete units such as capsules, cachets or tablets, each containing a predetermined amount of the active ingredient; as a powder or granules; as a solution or a suspension in an aqueous liquid or a non-aqueous liquid; or as an oil-in-water liquid emulsion or a water-in-oil liquid emulsion. The active ingredient may also be presented as a bolus, electuary or paste.

A tablet may be made by compression or moulding, optionally with one or more accessory ingredients. Compressed tablets may be prepared by compressing in a suitable machine the active ingredient in a free-flowing form such as a powder or granules, optionally mixed with a binder (eg povidone, gelatin, hydroxypropylmethyl cellulose), lubricant, inert diluent, preservative, disintegrant (eg sodium starch glycolate, cross-linked povidone, cross-linked sodium carboxymethyl cellulose), surface-active or dispersing agent. Moulded tablets may be made by moulding in a suitable machine a mixture of the powdered compound moistened with an inert liquid diluent. The tablets may optionally be coated or scored and may be formulated so as to provide slow or controlled release of the active ingredient therein using, for example, hydroxypropylmethylcellulose in varying proportions to provide desired release profile.

Formulations suitable for topical administration in the mouth include lozenges comprising the active ingredient in a flavoured basis, usually sucrose and acacia or tragacanth; pastilles comprising the active ingredient in an inert basis such as gelatin and glycerin, or sucrose and acacia; and mouth-washes comprising the active ingredient in a suitable liquid carrier.

Formulations suitable for parenteral administration include aqueous and non-aqueous sterile injection solutions which may contain anti-oxidants, buffers, bacteriostats and solutes which render the formulation isotonic with the blood of the intended recipient; and aqueous and non-aqueous sterile suspensions which may include suspending agents and thickening agents. The formulations may be presented in unit-dose or multi-dose containers, for example sealed ampoules and vials, and may be stored in a freeze-dried (lyophilised) condition requiring only the addition of the sterile liquid carrier, for example water for injections, immediately prior to use. Extemporaneous injection solutions and suspensions may be prepared from sterile powders, granules and tablets of the kind previously described.

Preferred unit dosage formulations are those containing a daily dose or unit, daily sub-dose or an appropriate fraction thereof, of an active ingredient.

It should be understood that in addition to the ingredients particularly mentioned above the formulations of this invention may include other agents conventional in the art having regard to the type of formulation in question, for example those suitable for oral administration may include flavouring agents.

A further aspect of the invention provides a method of affecting cellular metabolism or function, the method comprising administering to a cell (a) a compound which modulates the interaction between a PP1c and a regulatory subunit thereof or (b) a compound which mimics the effect of a regulatory subunit of PP1c or (c) a peptide capable of binding a PP1c and which affects the ability of PP1c to bind to a particular target and/or affects the regulation of PP1c activity, or a functional equivalent thereof.

It will be appreciated that the said compounds are disclosed above with respect to specific compounds or with respect to methods of obtaining such compounds.

In particular, it is preferred if the compound administered to the cell is any one or more of the peptides [G63-T93], [G63-N75], [E2-R575], [E2-P243], [E2-D118], [H100-P350] and peptide 63-80 of G_M or functional equivalents thereof or peptides comprising said peptide sequences or any one or more of the peptides [M1-E309], [M1-F38], [M1-A150] or [L24-Y496] of M_{110} or functional equivalents thereof or peptides comprising said peptide sequences. Preferably, the peptide is not [E2-R575] or [H100-P350].

In this embodiment it will be appreciated that functional equivalents include those compounds defined above as being functional equivalents, in particular, derivatives of peptides which are more readily able to enter a cell.

The compound may be administered to the cell in any suitable way, in particular in such a way that the compound will enter the cell in a suitable form to have its desired effect. Method of facilitating the entry of a compound into the cell are known in the art, for example, in relation to peptides the importins and penetrations may be used, or the peptides may be micro-injected or they may enter the cell in a suitable vehicle such as in a liposome.

Preferably, the cell is a cell in a mammalian body.

The aforementioned compounds of the invention or a formulation thereof may be administered by any conventional method including oral and parenteral (eg subcutaneous or intramuscular) injection. The treatment may consist of a single dose or a plurality of doses over a period of time.

Whilst it is possible for a compound of the invention to be administered alone, it is preferable to present it as a pharmaceutical formulation, together with one or more acceptable carriers. The carrier(s) must be "acceptable" in the sense of being compatible with the compound of the invention and not deleterious to

the recipients thereof. Typically, the carriers will be water or saline which will be sterile and pyrogen free.

A further aspect of the invention provides a method of treating a patient in need of modulation of PP1c activity or function the method comprising administering to the patient an effective amount of a compound which modulates the interaction between a PP1c and a regulatory subunit thereof or (b) a compound which mimics the effect of a regulatory subunit of PP1c or (c) a peptide capable of binding a PP1c and which affects the ability of PP1c to bind to a particular target and/or affects the regulation of PP1c activity, or a functional equivalent thereof.

As will be apparent from what is described herein, protein phosphatase-1 (PP1) is one of the principal serine/threonine-specific protein phosphatases in human cells where it plays key roles in regulating a variety of physiological roles, including the metabolism of glycogen, the splicing of mRNA, the exit from mitosis and the contraction of smooth muscle. The different functions of PP1 are carried out by distinct species of this enzyme in which the same catalytic unit is complexed to different "targeting" subunits. The latter class of proteins direct PP1 to specific subcellular loci, tailor its properties to the needs of a particular locus and confer the ability to be regulated by extracellular signals (hormones, growth factors, neurotransmitters). Compounds as herein described that disrupt specific PP1-"targeting" subunits interactions or mimic the effect of a targeting subunit are likely to have a number of therapeutic uses as outlined below.

PP1 interacts with the M110-subunit which targets it to myosin in smooth muscle and enhances the rate at which PP1 dephosphorylates myosin. The dephosphorylation of myosin underlies the relaxation of smooth muscle. Thus compounds such as those disclosed herein which disrupt the interaction of PP1

with M110 in arterial muscle are expected to increase the phosphorylation of arterial myosin and elevate blood pressure.

The interaction of PP1 with M110 enhances the rate at which PP1 dephosphorylates myosin, but suppresses the rate at which it dephosphorylates glycogen phosphorylase. The disruption of the PP1-M110 interaction is therefore measured in a screen by looking for compounds which enhance the dephosphorylation of phosphorylase and/or suppress the dephosphorylation of the myosin P-light chain (see the Examples).

Compounds, such as those disclosed herein, that mimic the effect of the M110 subunit in stimulating myosin dephosphorylation are expected to be useful in lowering blood pressure. Such compounds are identified by their ability to stimulate the dephosphorylation of the myosin P-light chain by the catalytic subunit of PP1. An example of such an assay, which shows that the N-terminal 38 residues of the M110 subunit stimulate the dephosphorylation of the myosin P-light chain by PP1, is shown in the Examples.

The interaction of PP1 with G_L targets the phosphatase to liver glycogen. This interaction enhances the dephosphorylation glycogen synthase which stimulates the conversion of glucose to glycogen. A compounds, such as those disclosed herein, disrupts the interaction between PP1 and G_L is expected to be useful in treating hypoglycaemia. The interaction of G_L with PP1 strongly suppresses the rate at which PP1 dephosphorylates glycogen phosphorylase. A compound, such as those disclosed herein, which disrupts the interaction of PP1 with G_L can be screened for very simply by its ability to increase the phosphorylase phosphatase activity of PP1 G_L. This can be carried out, for example, using rat liver glycogen pellet as described in the Examples. There is no need to use the purified enzyme.

PP1 interacts with p53 BP2 (Helps *et al*, 1995) a protein which is known to interact with the tumour suppressor p53. The phosphorylation of p53 is known to enhance its ability to bind to DNA and hence its ability to function as a tumour suppressor. p53BP2 may be a protein which targets PP1 to p53 stimulating the dephosphorylation and inactivation of p53. A compound, such as those disclosed herein, which disrupts the interaction of PP1 with p53BP2 may enhance the phosphorylation of p53 and its ability to function as a tumour suppressor. Since p53BP2 suppresses the dephosphorylation of glycogen phosphorylase (Helps *et al*, 1995), compounds that disrupt the p53BP2-PP1 complex can be screened by measuring the increase in rate of dephosphorylation of glycogen phosphorylase.

The present invention provides peptides able to bind to the catalytic sub-unit of protein phosphatase-1 (hereinafter referred to as PP1c). Generally the peptides affect the ability of PP1c to bind to particular target(s) and/or the regulation of PP1c activity.

Peptides can be designed based on the sequences of regulatory subunits, especially in relation to the peptide consensus sequence found therein and its flanking sequences. Peptides can be synthesised by methods well known in the art. For example, peptides may be synthesised by the Fmoc-polyamide mode of solid-phase peptide synthesis as disclosed by Lu *et al* (1981) *J. Org. Chem.* **46**, 3433 and references therein. Temporary N-amino group protection is afforded by the 9-fluorenylmethyloxycarbonyl (Fmoc) group. Repetitive cleavage of this highly base-labile protecting group is effected using 20% piperidine in N,N-dimethylformamide. Side-chain functionalities may be protected as their butyl ethers (in the case of serine threonine and tyrosine), butyl esters (in the case of glutamic acid and aspartic acid), butyloxycarbonyl derivative (in the case of lysine and histidine), trityl derivative (in the case of cysteine) and 4-methoxy-2,3,6-trimethylbenzenesulphonyl derivative (in the case

of arginine). Where glutamine or asparagine are C-terminal residues, use is made of the 4,4'-dimethoxybenzhydryl group for protection of the side chain amido functionalities. The solid-phase support is based on a polydimethyl-acrylamide polymer constituted from the three monomers dimethylacrylamide (backbone-monomer), bisacryloylethylene diamine (cross linker) and acryloylsarcosine methyl ester (functionalising agent). The peptide-to-resin cleavable linked agent used is the acid-labile 4-hydroxymethyl-phenoxyacetic acid derivative. All amino acid derivatives are added as their preformed symmetrical anhydride derivatives with the exception of asparagine and glutamine, which are added using a reversed N,N-dicyclohexyl-carbodiimide/1-hydroxybenzotriazole mediated coupling procedure. All coupling and deprotection reactions are monitored using ninhydrin, trinitrobenzene sulphonic acid or isotin test procedures. Upon completion of synthesis, peptides are cleaved from the resin support with concomitant removal of side-chain protecting groups by treatment with 95% trifluoroacetic acid containing a 50% scavenger mix. Scavengers commonly used are ethanedithiol, phenol, anisole and water, the exact choice depending on the constituent amino acids of the peptide being synthesised. Trifluoroacetic acid is removed by evaporation *in vacuo*, with subsequent trituration with diethyl ether affording the crude peptide. Any scavengers present are removed by a simple extraction procedure which on lyophilisation of the aqueous phase affords the crude peptide free of scavengers. Reagents for peptide synthesis are generally available from Calbiochem-Novabiochem (UK) Ltd, Nottingham NG7 2QJ, UK. Purification may be effected by any one, or a combination of, techniques such as size exclusion chromatography, ion-exchange chromatography and (principally) reverse-phase high performance liquid chromatography. Analysis of peptides may be carried out using thin layer chromatography, reverse-phase high performance liquid chromatography, amino-acid analysis after acid hydrolysis and by fast atom bombardment (FAB) mass spectrometric analysis.

The peptides may be derived from the targeting subunit(s) of PP1c, in particular from the subunits G_L, G_M, M_{110} and/or M_{21}. Additionally the peptides may be derived from other subunits such as different M-complexes, p53BP2, sds22, NIPP1, L5, Inhibitor-1, Inhibitor-2, DARPP or the like. Functional equivalents or portions of these peptides may also be used.

In a further aspect the present invention provides the use of peptides derived from targeting subunit(s) of PP1c, functional equivalents or portions thereof to affect cellular metabolism or function.

In a further aspect the present invention provides a method of treatment of the human or non-human (preferably mammalian) animal body, said method comprising altering the levels of peptides derived from targeting subunit(s) of PP1c, functional equivalents or portions thereof to an extent that cellular metabolism or function is affected.

Aspects of cellular metabolism that may be affected include (but are not limited to) glycogen metabolism, muscle metabolism, physiology and function.

Generally the levels of peptides or their activity will be enhanced in cells and this control may be achieved by causing higher levels of expression of nucleotides sequences encoding for such peptides (optionally linked to molecules which allow them to cross a cell membrane) or through the administration of such peptides or precursors thereof. Alternatively, in some circumstances, it may be more desirable to depress the levels of certain peptides or at least to depress the level of peptides in active form.

Preferred peptides according to the present invention are derivatives of G_M, especially [G63-T93], [G63-N75], [E2-R575], [E2-P243], [E2-D118], [H100-P350] and peptide 63 to 80, and derivatives of M_{110}, especially

[M1-E309], [M1-F38], [M1-A150], [L24-Y496]. Preferably, the peptide is not [E2-R575] or [H100-P350].

Particularly preferred peptides are those derived from amino acid nos. 63 to 93 (including 63-80 and 63-75) of G_M; or from amino acids 1 to 309 (including from 1-150 and 1-38) of M_{110}.

The sequence of G_M is given in Chen *et al* (1994) *Diabetes* 43, 1234-1241.

In yet further aspect the present invention provides chimeric proteins containing portions of other proteins or peptides or containing additional amino acids.

Additionally the present invention provides nucleotide sequences (optionally in the form of plasmids) encoding the peptides or chimeric proteins of interest. DNA which encodes the polypeptides or peptides of the invention or chimeric proteins can be made based on a knowledge of the peptide sequences disclosed herein. The DNA is then expressed in a suitable host to produce a polypeptide comprising the compound of the invention. Thus, the DNA encoding the polypeptide constituting the compound of the invention may be used in accordance with known techniques, appropriately modified in view of the teachings contained herein, to construct an expression vector, which is then used to transform an appropriate host cell for the expression and production of the polypeptide of the invention. Such techniques include those disclosed in US Patent Nos. 4,440,859 issued 3 April 1984 to Rutter *et al*, 4,530,901 issued 23 July 1985 to Weissman, 4,582,800 issued 15 April 1986 to Crowl, 4,677,063 issued 30 June 1987 to Mark *et al*, 4,678,751 issued 7 July 1987 to Goeddel, 4,704,362 issued 3 November 1987 to Itakura *et al*, 4,710,463 issued 1 December 1987 to Murray, 4,757,006 issued 12 July 1988 to Toole, Jr. *et al*, 4,766,075 issued 23 August 1988 to Goeddel *et al* and 4,810,648 issued 7 March 1989 to Stalker, all of which are incorporated herein by reference.

The DNA encoding the polypeptide constituting the compound of the invention may be joined to a wide variety of other DNA sequences for introduction into an appropriate host. The companion DNA will depend upon the nature of the host, the manner of the introduction of the DNA into the host, and whether episomal maintenance or integration is desired.

Generally, the DNA is inserted into an expression vector, such as a plasmid, in proper orientation and correct reading frame for expression. If necessary, the DNA may be linked to the appropriate transcriptional and translational regulatory control nucleotide sequences recognised by the desired host, although such controls are generally available in the expression vector. The vector is then introduced into the host through standard techniques. Generally, not all of the hosts will be transformed by the vector. Therefore, it will be necessary to select for transformed host cells. One selection technique involves incorporating into the expression vector a DNA sequence, with any necessary control elements, that codes for a selectable trait in the transformed cell, such as antibiotic resistance. Alternatively, the gene for such selectable trait can be on another vector, which is used to co-transform the desired host cell.

Host cells that have been transformed by the recombinant DNA of the invention are then cultured for a sufficient time and under appropriate conditions known to those skilled in the art in view of the teachings disclosed herein to permit the expression of the polypeptide, which can then be recovered.

Many expression systems are known, including bacteria (for example *E. coli* and *Bacillus subtilis*), yeasts (for example *Saccharomyces cerevisiae*), filamentous fungi (for example *Aspergillus*), plant cells, animal cells and insect cells.

The vectors include a prokaryotic replicon, such as the ColE1 *ori*, for

propagation in a prokaryote, even if the vector is to be used for expression in other, non-prokaryotic, cell types. The vectors can also include an appropriate promoter such as a prokaryotic promoter capable of directing the expression (transcription and translation) of the genes in a bacterial host cell, such as *E. coli*, transformed therewith.

A promoter is an expression control element formed by a DNA sequence that permits binding of RNA polymerase and transcription to occur. Promoter sequences compatible with exemplary bacterial hosts are typically provided in plasmid vectors containing convenient restriction sites for insertion of a DNA segment of the present invention.

Typical prokaryotic vector plasmids are pUC18, pUC19, pBR322 and pBR329 available from Biorad Laboratories, (Richmond, CA, USA) and p*Trc*99A and pKK223-3 available from Pharmacia, Piscataway, NJ, USA.

A typical mammalian cell vector plasmid is pSVL available from Pharmacia, Piscataway, NJ, USA. This vector uses the SV40 late promoter to drive expression of cloned genes, the highest level of expression being found in T antigen-producing cells, such as COS-1 cells.

An example of an inducible mammalian expression vector is pMSG, also available from Pharmacia. This vector uses the glucocorticoid-inducible promoter of the mouse mammary tumour virus long terminal repeat to drive expression of the cloned gene.

Useful yeast plasmid vectors are pRS403-406 and pRS413-416 and are generally available from Stratagene Cloning Systems, La Jolla, CA 92037, USA. Plasmids pRS403, pRS404, pRS405 and pRS406 are Yeast Integrating plasmids (YIps) and incorporate the yeast selectable markers *HIS3*, *TRP1*,

LEU2 and *URA3*. Plasmids pRS413-416 are Yeast Centromere plasmids (YCps)

A variety of methods have been developed to operably link DNA to vectors via complementary cohesive termini. For instance, complementary homopolymer tracts can be added to the DNA segment to be inserted to the vector DNA. The vector and DNA segment are then joined by hydrogen bonding between the complementary homopolymeric tails to form recombinant DNA molecules.

Synthetic linkers containing one or more restriction sites provide an alternative method of joining the DNA segment to vectors. The DNA segment, generated by endonuclease restriction digestion as described earlier, is treated with bacteriophage T4 DNA polymerase or *E. coli* DNA polymerase I, enzymes that remove protruding, 3'-single-stranded termini with their 3'-5'-exonucleolytic activities, and fill in recessed 3'-ends with their polymerizing activities.

The combination of these activities therefore generates blunt-ended DNA segments. The blunt-ended segments are then incubated with a large molar excess of linker molecules in the presence of an enzyme that is able to catalyze the ligation of blunt-ended DNA molecules, such as bacteriophage T4 DNA ligase. Thus, the products of the reaction are DNA segments carrying polymeric linker sequences at their ends. These DNA segments are then cleaved with the appropriate restriction enzyme and ligated to an expression vector that has been cleaved with an enzyme that produces termini compatible with those of the DNA segment.

Synthetic linkers containing a variety of restriction endonuclease sites are commercially available from a number of sources including International Biotechnologies Inc, New Haven, CN, USA.

A desirable way to modify the DNA encoding the polypeptide of the invention is to use the polymerase chain reaction as disclosed by Saiki *et al* (1988) *Science* 239, 487-491.

In this method the DNA to be enzymatically amplified is flanked by two specific oligonucleotide primers which themselves become incorporated into the amplified DNA. The said specific primers may contain restriction endonuclease recognition sites which can be used for cloning into expression vectors using methods known in the art. In relation to the above section on DNA expression the term "polypeptide" includes peptides and chimeric proteins.

Further the present invention provides host cells transformed with suitable expression vectors and able to express the peptides. The host cells may be prokaryotic (e.g. *E. coli*) or eukaryotic (e.g. yeast, mammalian cell cultures).

Bacterial cells are preferred prokaryotic host cells and typically are a strain of *E. coli* such as, for example, the *E. coli* strains DH5 available from Bethesda Research Laboratories Inc., Bethesda, MD, USA, and RR1 available from the American Type Culture Collection (ATCC) of Rockville, MD, USA (No ATCC 31343). Preferred eukaryotic host cells include yeast and mammalian cells, preferably vertebrate cells such as those from a mouse, rat, monkey or human fibroblastic cell line. Yeast host cells include YPH499, YPH500 and YPH501 which are generally available from Stratagene Cloning Systems, La Jolla, CA 92037, USA. Preferred mammalian host cells include Chinese hamster ovary (CHO) cells available from the ATCC as CCL61, NIH Swiss mouse embryo cells NIH/3T3 available from the ATCC as CRL 1658, and monkey kidney-derived COS-1 cells available from the ATCC as CRL 1650.

Transformation of appropriate cell hosts with a DNA construct of the present

invention is accomplished by well known methods that typically depend on the type of vector used. With regard to transformation of prokaryotic host cells, see, for example, Cohen *et al* (1972) *Proc. Natl. Acad. Sci. USA* **69**, 2110 and Sambrook *et al* (1989) *Molecular Cloning, A Laboratory Manual*, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY. Transformation of yeast cells is described in Sherman *et al* (1986) *Methods In Yeast Genetics, A Laboratory Manual*, Cold Spring Harbor, NY. The method of Beggs (1978) *Nature* **275**, 104-109 is also useful. With regard to vertebrate cells, reagents useful in transfecting such cells, for example calcium phosphate and DEAE-dextran or liposome formulations, are available from Stratagene Cloning Systems, or Life Technologies Inc., Gaithersburg, MD 20877, USA.

Electroporation is also useful for transforming cells and is well known in the art for transforming yeast cell, bacterial cells and vertebrate cells.

For example, many bacterial species may be transformed by the methods described in Luchansky *et al* (1988) *Mol. Microbiol.* **2**, 637-646 incorporated herein by reference. The greatest number of transformants is consistently recovered following electroporation of the DNA-cell mixture suspended in 2.5X PEB using 6250V per cm at 25μFD.

Methods for transformation of yeast by electroporation are disclosed in Becker & Guarente (1990) *Methods Enzymol.* **194**, 182.

Successfully transformed cells, ie cells that contain a DNA construct of the present invention, can be identified by well known techniques. For example, cells resulting from the introduction of an expression construct of the present invention can be grown to produce the polypeptide of the invention. Cells can be harvested and lysed and their DNA content examined for the presence of the DNA using a method such as that described by Southern (1975) *J. Mol. Biol.*

98, 503 or Berent *et al* (1985) *Biotech.* 3, 208. Alternatively, the presence of the protein in the supernatant can be detected using antibodies as described below.

In addition to directly assaying for the presence of recombinant DNA, successful transformation can be confirmed by well known immunological methods when the recombinant DNA is capable of directing the expression of the protein. For example, cells successfully transformed with an expression vector produce proteins displaying appropriate antigenicity. Samples of cells suspected of being transformed are harvested and assayed for the protein using suitable antibodies.

Thus, in addition to the transformed host cells themselves, the present invention also contemplates a culture of those cells, preferably a monoclonal (clonally homogeneous) culture, or a culture derived from a monoclonal culture, in a nutrient medium.

In another aspect the present invention provides antibodies to PP1c which act in an analogous manner to the peptides of interest. Antibodies to the peptides themselves are also provided and these may themselves be used to affect cell metabolism or function.

Peptides in which one or more of the amino acid residues are chemically modified, before or after the peptide is synthesised, may be used providing that the function of the peptide, namely the production of specific antibodies *in vivo*, remains substantially unchanged. Such modifications include forming salts with acids or bases, especially physiologically acceptable organic or inorganic acids and bases, forming an ester or amide of a terminal carboxyl group, and attaching amino acid protecting groups such as N-t-butoxycarbonyl. Such modifications may protect the peptide from *in vivo* metabolism. The peptides

may be present as single copies or as multiples, for example tandem repeats. Such tandem or multiple repeats may be sufficiently antigenic themselves to obviate the use of a carrier. It may be advantageous for the peptide to be formed as a loop, with the N-terminal and C-terminal ends joined together, or to add one or more Cys residues to an end to increase antigenicity and/or to allow disulphide bonds to be formed. If the peptide is covalently linked to a carrier, preferably a polypeptide, then the arrangement is preferably such that the peptide of the invention forms a loop.

According to current immunological theories, a carrier function should be present in any immunogenic formulation in order to stimulate, or enhance stimulation of, the immune system. It is thought that the best carriers embody (or, together with the antigen, create) a T-cell epitope. The peptides may be associated, for example by cross-linking, with a separate carrier, such as serum albumins, myoglobins, bacterial toxoids and keyhole limpet haemocyanin. More recently developed carriers which induce T-cell help in the immune response include the hepatitis-B core antigen (also called the nucleocapsid protein), presumed T-cell epitopes such as Thr-Ala-Ser-Gly-Val-Ala-Glu-Thr-Thr-Asn-Cys (SEQ ID No 1), beta-galactosidase and the 163-171 peptide of interleukin-1. The latter compound may variously be regarded as a carrier or as an adjuvant or as both. Alternatively, several copies of the same or different peptides of the invention may be cross-linked to one another; in this situation there is no separate carrier as such, but a carrier function may be provided by such cross-linking. Suitable cross-linking agents include those listed as such in the Sigma and Pierce catalogues, for example glutaraldehyde, carbodiimide and succinimidyl 4-(N-maleimidomethyl)cyclohexane-1-carboxylate, the latter agent exploiting the -SH group on the C-terminal cysteine residue (if present).

If the peptide is prepared by expression of a suitable nucleotide sequence in a suitable host, then it may be advantageous to express the peptide as a fusion

product with a peptide sequence which acts as a carrier. Kabigen's "Ecosec" system is an example of such an arrangement.

The peptide of the invention may be linked to other antigens to provide a dual effect.

In a yet further aspect the present invention provides a method of diagnosis of abnormalities of cellular metabolism, said method comprising analysing the naturally occurring peptide(s) or the nucleotide sequences encoding therefore and comparing the results to the peptides described herein.

The peptides of the present invention may also be used in diagnosis and this aspect is also covered by the present invention.

The specificity of the catalytic subunit of protein phosphatase-1 (PP1c) is modified by regulatory subunits that target it to particular subcellular locations. For the first time we have identified PP1c-binding domains on G_L and G_M, the subunits that target PP1c to hepatic and muscle glycogen, respectively, and on M_{110}, the subunit that targets PP1c to smooth muscle myosin. The peptide G_M-(G63-T93) interacted with PP1c and prevented G_L from suppressing the dephosphorylation of glycogen phosphorylase, but it did not dissociate G_L from PP1c or affect other characteristic properties of the $PP1_{GL}$ complex. These results indicate that G_L contains two PP1c-binding sites, the region which suppresses the dephosphorylation of glycogen phosphorylase being distinct from that which enhances the dephosphorylation of glycogen synthase. At higher concentrations, G_M-(G63-N75) had the same effect as G_M-(G63-T93), but not if Ser67 was phosphorylated by cyclic AMP-dependent protein kinase. Thus phosphorylation of Ser67 dissociates G_M from PP1c because phosphate is inserted into the PP1c-binding domain of G_M. The fragments M_{110}-(M1-E309) and M_{110}-(M1-F38), but not M_{110}-(D39-E309), mimicked the M_{110} subunit in

stimulating dephosphorylation of the smooth muscle myosin P-light chain and heavy meromyosin *in vitro*. However, in contrast to the M_{110} subunit and M_{110}-(M1-E309), neither M_{110}-(M1-F38) nor M_{110}-(D39-E309) suppressed the PP1c-catalysed dephosphorylation of glycogen phosphorylase. These observations suggest that the region which stimulates the dephosphorylation of myosin is situated within the N-terminal 38 residues of the M_{110} subunit, while the region which suppresses the dephosphorylation of glycogen phosphorylase requires the presence of at least part of the region 39-296 which contains seven ankyrin repeats. M_{110}-(M1- F38) displaced G_L from PP1c, while G_M-(G63-T93) displaced M_{110} from PP1c *in vitro*. These observations indicate that the region(s) of PP1c that interact with G_M/G_L and M_{110} overlap, explaining why different forms of PP1c contain just a single targeting subunit.

We also disclose the structure of PP1c in complex with a portion of a targeting subunit, and show that changing key amino acid residues in the subunit disrupts its interaction with PP1c. These studies identify a critical structural motif in targeting subunits involved in the interaction with PP1c as well as the recognition site on PP1c itself. These findings will facilitate the rational design of agents such as peptides or other forms of small cell-permeant molecules that act by disrupting PP1-targeting subunit interactions. Given the structural motif and the coordinates of the atoms in the crystal structure, it is within the scope of the abilities of a skilled molecular modeller to produce small cell-permeant molecules, which can enter cells naturally, and possess either the same motif, or an analogous structure to give the same functional properties to the molecule. Thus the small cell-permeant molecule can have a precise copy of the motif, or one which is functionally equivalent. The molecule can be a peptide, but other types of molecules, which are transferred across the plasma membrane of cells, may be preferred.

Several mammalian PP1c targeting subunits have been isolated and

characterised, including the G_M subunit that targets PP1c to both the glycogen particles and sarcoplasmic reticulum of striated muscles (Tang *et al.*, 1991; Chen *et al.*, 1994), the G_L subunit that targets PP1c to liver glycogen (Moorhead *et al.*, 1995; Doherty *et al.*, 1995), the M_{110} subunits responsible for the association of PP1c with the myofibrils of skeletal muscle (Moorhead *et al.*, 1994; Alessi *et al.*, 1992) and smooth muscle (Alessi *et al.*, 1992; Chen *et al.*, 1994), the p53 binding protein p53BP2 (Helps *et al.*, 1995) and the nuclear protein NIPP-1 (Jagiello *et al.*, 1995; Van Eynde *et al.*, 1995). PP1c is also reported to interact with other mammalian proteins such as the retinoblastoma gene product (Durphee *et al.*, 1993), an RNA splicing factor (Hirano *et al.*, 1996), ribosomal proteins L5 (Hirano *et al.*, 1995) and RIPP-1 (Beullens *et al.*, 1996), a 110 kDa nuclear protein yet to be identified (Jagiello *et al.*, 1995), kinesin-like proteins and small cytosolic proteins, inhibitor-1, DARPP-32 and inhibitor-2 (Cohen, 1989; Cohen, 1992, Hubbard and Cohen, 1993). Moreover, a number of distinct PP1-regulatory subunits have been identified in yeast (reviewed by Stark, 1996). We attempted to identify which regions of the G_M and M_{110} subunits were involved in binding to PP1c. These studies led to the identification of relatively small peptides from each targeting subunit that were capable of interacting with PP1c. Peptides comprising residues 63-93, 63-80 and 63-75 of G_M bound to PP1c, dissociating it from G_L, while the N-terminal 38 residues of the M_{110} subunit (M_{110}[1-38]) mimicked the intact M_{110} subunit in enhancing the rate at which PP1c dephosphorylated the 20 kDa myosin light chain (MLC_{20}) subunit of smooth muscle myosin (Johnson *et al.*, 1996).

The present invention thus provides peptides comprising the N-terminal 38 residues of the M_{110} subunit, and those comprising residues 63-93, 63-80 and 63-75 of G_M.

Phosphorylation of Ser 67 of G_M by protein kinase A (PKA) disrupts the

interaction of G_M with PP1c (Dent *et al.*, 1990) and a similar disruption is also observed following the phosphorylation of Ser 67 of the G_M[63-75] peptide (Johnson *et al.*, 1996). The finding that G_M[63-93] disrupted the interaction between PP1c and the M_{110} subunit, and prevented M_{110} from enhancing the MLC_{20} phosphatase activity of PP1c implies that the binding of M_{110} and G_M to PP1c are mutually exclusive.

Thus the invention contemplates the substitution or modification of an amino acid in any such peptide.

To understand the basis for the recognition by PP1c of regulatory subunits, and peptides derived from these subunits, we co-crystallised a complex of PP1c with the G_M[63-75] peptide and determined the structure at 3.0 Å resolution. These experiments have demonstrated that residues 64 to 69 of the peptide are bound in an extended conformation to a hydrophobic channel within the C-terminal region of PP1c. The residues in G_M[63-75] that interact with PP1c lie in an Arg/Lys-Val/Ile--Xaa-Phe motif common to M_{110}[1-38] and almost all known mammalian PP1-binding proteins. Substituting Val or Phe by Ala in the G_M[63-75] peptide, and deleting the VxF motif from the M_{110}[1-38] peptide, abolished the ability of both peptides to interact with PP1c. These findings identify a recognition site on PP1c for a critical structural motif involved in the interaction of targeting subunits with PP1.

Particularly preferred peptides are derived from residues 63 to 69 of G_M and comprise the motif Arg/Lys-Val/Ile-Xaa-Phe. Peptides derived from M_{110} (or any other source) and also including the motif are also included in the scope of the invention.

Preferred peptides may also be substantially or wholly made up of hydrophobic residues.

The identification of this area of PP1c necessary for binding to the various subunits allows the design of agents to specifically disrupt the interaction at this area. Such disruption may, for example, increase the phosphorylation of the protein phospholamban in cardiac muscle and thus increase the force and rate of contraction of the muscle. This provides a possible treatment for congestive heart failure. Also, the specific disruption of the complex of PP1 and p53BP2 may prevent PP1 from dephosphorylating the tumour suppressor protein p53, thus enhancing phosphorylation of p53, its ability to bind to DNA, and thus its ability to act as a tumour suppressor.

The identification of the key motif in targetting subunits that bind to PP1 also provides the means to produce targetting subunits that can no longer interact with PP1. Over-expression of these mutant targetting subunits provides a powerful new way to determine the functions of different targetting subunits *in vivo*.

Abbreviations

PP1, protein phosphatase-1
PP1c, catalytic subunit of PP1
PP1, -isoform of PP1c
$PP1_G$, glycogen-associated form of PP1
$PP1_M$, myosin-associated form of PP1
G_M, glycogen-binding subunit of PP1 from striated muscle
G_L, glycogen-binding subunit of PP1 from liver
NIPP1, nuclear inhibitor of PP1
DARPP, dopamine and cyclic AMP-regulated phosphoprotein
M_{21} and M_{110}, myofibrillar-binding subunits of PP1 with molecular masses of 21kDa and 110 kDa respectively.

PKA, cyclic AMP-dependent protein kinase
PhMeSO_2F, phenylmethylsuphonyl fluoride
GST, glutathione-S-transferase
MLC_{20}, myosin light chain of molecular mass 20 kDa.

The invention is now described in more detail by reference to the following Examples and Figures wherein:

Figure 1 shows that the N-terminal 118 residues of human G_M interact with PP1c.

GST-G_M fusion proteins were electrophoresed on 10% SDS/polyacrylamide gels and stained with Coomassie blue (lanes 1-3) or, after transfer to nitrocellulose, probed with digoxygenin-labelled PP1γ (lanes 4-6) as in [9]. Lanes 1 and 4, GST-G_M-(E2-D118); Lanes 2 and 5, GST-G_M-(H100-P350); Lanes 3 and 6, GST. The positions of the marker proteins glycogen phosphorylase (97 kDa), bovine serum albumin (66 kDa), ovalbumin (43 kDa), carbonic anhydrase (29 kDa) and soybean trypsin inhibitor (20 kDa) are indicated.

Figure 2 shows that synthetic peptides between residues 63 and 93 of rabbit G_M stimulate the phosphorylase phosphatase activity of $PP1_{GL}$.

Hepatic glycogen particles were diluted in assay buffer to 0.6 phosphorylase phosphatase (PhP) mU per ml, incubated for 15 minutes at 30°C with G_M-(G63-T93) (closed circles), G_M-(G63-K80) (open circles) or G_M-(G63-N75) (closed triangles) and assayed as described in Example 1. The open triangles show the effect of G_M-(G63-N75) which had been phosphorylated at Ser67 by PKA (pG_M-(G63-N75)). Similar results were obtained in four experiments.

Figure 3 shows that removal of the M_{21} subunit from smooth muscle $PP1_M$ does

not affect its MLC_{20} phosphatase:phosphorylase phosphatase activity ratio.

(A) Purified smooth muscle $PP1_M$ was electrophoresed on a 12% SDS/polyacrylamide gel, and either stained with Coomassie blue (lane 1) or immunoblotted [32] with antibodies specific for the M_{21} subunit (lane 2) or the M_{110} subunit (lane 3). The positions of the M_{110} subunit, the M_{21} subunit and PP1c are marked.

(B) Purified $PP1_M$ (lane 1) or $PP1_M$ lacking the M_{21} subunit (lane 2) were electrophoresed on a 12% SDS polyacrylamide gel, transferred to nitrocellulose and immunoblotted with mixed, affinity-purified antibodies to the M_{110} and M_{21} subunits. The M_{110} and M_{21} subunits are marked. The activity ratio, MLC_{20} phosphatase (MP):phosphorylase phosphatase (PhP) of the two preparations is also shown. Similar results were obtained in three different experiments. The activity ratio MP:PhP of PP1c is 0.07.

Figure 4 shows expressed fragments of the M_{110} subunit before and after cleavage of the GST-fusion proteins with thrombin .

Purified GST-fusion proteins were electrophoresed on a 15% SDS/polyacrylamide gel and stained with Coomassie blue. Lane 1, GST-M_{110}-(M1-A150); Lane 2, GST-M_{110}-(D39- E309); Lane 3, GST-M_{110}-(M1-E309); Lane 4, GST-M_{110}-(L24- Y496). Lanes 5-8 are the same as Lanes 1-4 except that the fusion proteins were cleaved with thrombin. The positions of the marker proteins glycogen phosphorylase (97 kDa), bovine serum albumin (66 kDa), ovalbumin (43 kDa), carbonic anhydrase (29 kDa), GST (26 kDa) and soybean trypsin inhibitor (20 kDa) are marked.

Figure 5 shows the effect of M_{110} subunit fragments on PP1c-catalysed dephosphorylation of MLC_{20} and glycogen phosphorylase

A,B; Effects of M_{110}-(M1-E309) (closed circles), M_{110}-(M1-F38) (open circles) and M_{110}-(D39-E309) (open triangles) on the MLC_{20} phosphatase (B) and phosphorylase phosphatase (B) activities of PP1c were measured after incubating PP1c for 15 minutes at 30°C with each fragment. The results are presented as a percentage of those obtained in experiments where the M_{110} fragments were omitted.

C,D; The effect of M_{110}-(M1-A150) (open circles) and M_{110}-(L24-Y496) (closed circles) on the MLC_{20} phosphatase (C) and phosphorylase phosphatase (D) activities of PP1c were measured as in A,B.

Figure 6 shows the effect of M_{110}-(M1-F38) and M_{110}-(M1-E309) on the dephosphorylation of glycogen synthase by PP1c.

The glycogen synthase phosphatase activity of PP1c was measured after a 15 minute incubation at 30°C with the indicated concentrations of M_{110}-(M1-F38) and M_{110}-(M1-E309). Similar results were obtained in three different experiments.

Figure 7 shows that G_M-(G63-T93) dissociates $PP1_M$.

(A) The phosphorylase phosphatase (PhP) activity of $PP1_M$ (closed circles) and its MLC_{20} phosphatase (MLCP) activity (open circles) were assayed after preincubation for 15 minutes at 30°C with the indicated concentrations of G_M-(G63-T93). Activities are shown relative to control incubations in which G_M-(G63-T93) was omitted. Similar results were obtained in three experiments.

(B,C) PPIM was incubated for 15 minutes at 30°C in the absence (B) and presence (C) of 10 M G_M-(G63-T93), then passed through a 30 x 1 cm column

of Superose 12 equilibrated at ambient temperature in 50 mM Tris/HC1 pH 7.5, 0.2M NaC1, 0.1 mM EGTA, 0.1% (by vol) 2-mercaptoethanol, 0.03% (by mass) Brij 35 in the absence (B) or presence (C) of 1 μM G_M-(G63-T93). Fractions (0.25 ml) were assayed for MLC_{20} phosphatase (MLCP) in B and for phosphorylase phosphatase (PhP) activity in C. The arrows denote the position of ferritin (450 kDa) and ovalbumin (43 kDa).

Figure 8 shows that G_M-(G63-T93) prevents M_{110}-(M1-F38) or M_{110}-(M1- E309) from modulating the substrate specificity of PP1c.

(A) The MLC_{20} phosphatase activity of PP1c was assayed after incubation for 15 minutes at 30°C in the presence or absence of 1 μM G_M-(G63-T93) and either 0.1 μM M_{110}-(M1-F38) or 0.1 nM M_{110}-(M1-E309).

(B) The phosphorylase phosphatase activity of PP1c was assayed as in A in the presence or absence of 1 μM G_M-(G63-T93) and 1.0 nM M_{110}-(M1-E309). The results are presented (SEM for three experiments) as a percentage of the PP1c activity measured in the absence of G_M-(63-T93), M_{110}-(M1-F38) or M_{110}-(M1-E309).

Figure 9 shows the location of PP1c-binding domains on the G_M and M_{110} targeting subunits and their effects on PP1 activity.

The hatched boxes in the M_{110} subunit denote the positions of the ankyrin repeats.

Figure 10 shows a stereo view of the electron density corresponding to the peptide. A: Initial 2-fold averaged electron map. B: map calculated using 3Fo-2Fc coefficients and phases calculated from the final refined model. Displayed using TURBO-FRODO.

Figure 11 shows the structure of PP1-G_M[63-75] peptide complex. A. Stereo view of a ribbons diagram of PP1c to indicate the position of the peptide binding channel at the interface of the two β-sheets of the β-sandwich. The peptide atoms are represented as ball-and-stick (MOLSCRIPT, Kraulis, 1991).

B. View of the surface of PP1c to show the hydrophobic peptide binding channel. Residues 63' to 69' (GRRVSFA) (SEQ ID No 2) of the G_M[63 75] peptide are shown as sticks. Drawn with TURBO-FRODO.

C. Stereo view of the G_M[63-75] peptide at the recognition site of PP1 to indicate polar interactions between peptide and protein and the formation of the β-sheet between Ser 67' - Ala 69' and 14 of PP1. Drawn with TURBO-FRODO.

D. Solvent accessible surface and surface electrostatic potential of PP1-G_M[63 75] peptide complex calculated with PP1 coordinates alone and showing the peptide as a stick representation in the vicinity of the peptide binding site. The figure was created with GRASP (Nicholls and Honig, 1991). The protein surface is coloured according to electrostatic potential from red (most negative) to blue (most positive). The figure shows pronounced negative electrostatic potential in the region surrounding the N-terminus of the peptide binding site that results from seven conserved acidic residues.

E. Details of the structure of the peptide binding site to show hydrophobic interactions between PP1c and Val 66', Phe 68' and Ala 69' of the G_M[68-75] peptide (MOLSCRIPT, Kraulis, 1991).

Figure 12 shows a sequence alignment of PP1-regulatory subunits in the vicinity of the (R/K)(V/I) x F motif. (A) mammalian PP1-binding subunits. G_M, Tang *et al.*, 1991; GL, Docherty *et al.*, 1995; G_L-related protein, Doherty

et al., 1996; p53BP2, Helps *et al.*, 1995; NIPP-1, Bollen *et al.*, 1995; splicing factor PSF, Hirano *et al.*, 1996; M_{110} subunit, Chen *et al.*, 1994; inhibitor-1, Aitken *et al.*, 1982; DARPP-32, Williams *et al.*, 1986. (B) PP1-binding proteins in *S. cerevisiae*. GACl (Francois *et al.*, 1992); PIG2 GIP1, GIP2, YIL045W (Tu *et al.*, 1996); REGl, REG2 (Tu and Carlson, 1995; Frederick and Tatchell, 1996); SCD5 (Nelson *et al* 1996; Tu *et al* 1996). The region homologous to the RRVSFA (SEQ ID No 3) motif in G_M which intersects with PP1c is boxed.

Figure 13 shows the disruption of the interactions between PP1c and the G_L and M_{110} subunits by a synthetic peptide from p53BP2. (A) $PP1_M$ from chicken gizzard smooth muscle (Alessi *et al.*, 1992) was diluted and incubated for 15 min at 30 °C with the peptide GKRTNLRKTGSERIAHGMRVKFNPLALLLDSC (SEQ ID No 4), corresponding to the sequence in p53BP2 that contains the RVxF motif. Reactions were started with either ^{32}P-labelled MLC_{20} or glycogen phosphorylase and the MLC_{20} phosphatase (open circles) and phosphorylase phosphatase (PhP, closed circles) activities were determined. The results are expressed as a percentage of the activity determined in control incubations where the p53BP2 peptide was omitted (100%). Similar results were obtained in three separate experiments. (B) same as (A) except that the peptide was incubated with diluted hepatic glycogen particles containing PP1-G_L before measuring the PhP activity. Similar results were obtained in three separate experiments.

Figure 14 shows the effect of M_{110}[M1-F38] and M_{110}[M1-K35] on the PP1c-catalysed dephosphorylation of MLC_{20} M_{110}[M1-F38] (1-38, open circles) or M_{110}[M1-K35] (1-35, closed circles) were incubated with PP1c for 15 min at 30°C and reactions started with the ^{32}P-labelled MLC_{20} substrate. The results are expressed as a % of the activity determined in control incubations where

the M_{110} peptides were omitted (100%). Similar results were obtained in three separate experiments.

Figure 15 shows the effect of synthetic peptides derived from the M_{110} and G_M subunits on the phosphorylase phosphatase activity of PP1-G_L. (A) Hepatic glycogen protein particles containing PP1-G_L were diluted and incubated for 15 min at 30°C with the indicated concentrations of either M_{110}[M1-F38] (open circles) or M_{110}[M1-K35] (closed circles) and the phosphatase reactions were initiated by addition of ^{32}P-labelled glycogen phosphorylase. The results are expressed as a percentage of the activity determined in control incubations where the M_{110} peptides were omitted. Similar results were obtained in three separate experiments. (B) The experiment was carried out as in (A), except that the peptide G_M[G63-N75] ("wild type", WT) and variants in which either Val 66 (V66A) (closed triangles) or Phe 68 (F68A) (closed circles) were changed to Ala, were used instead of the M_{110} peptides. Similar results were obtained in three separate experiments.

Figure 16 shows a stereo view of a ribbons diagram of a model of PP1-phospho-inhibitor-1 complex. The side chains of Ile 10, Phe 12 and pThr 35 of phospho-inhibitor-1 are shown with the main-chain atoms of residues 8 to 36 of the inhibitor indicated as a shaded ribbon. Drawn with MOLSCRIPT (Kraulis 1991).

Figure 17 shows a comparison of rat and chicken gizzard M_{110} and M_{21} subunits.

Vertical lines indicate identical residues, colons denote similar residues in the rat and chicken M_{110} sequences and deletions are shown by dots. (A) Comparison of M_{110} subunits. Underlined residues in the rat M_{110} subunit (Rat1) are deleted in some rat aorta forms and underlined residues in the

chicken M_{110} subunit (Ch1) are deleted in some chicken gizzard forms [5, 8]. Dashed lines above residues indicate amino acids deleted in the rat kidney M_{110} subunit [9]. The alternative C-terminal sequences of rat uterus M_{110} subunit are shown as Rat1 and Rat2. Leucine residues in the C-terminal leucine zipper motif are double underlined. (B). The C-terminal sequence of the M_{110} subunit is structurally related to the M_{21} subunit. The sequence of the chicken M_{21} subunit [5] is compared with the C-terminal sequences of Rat2 and Ch1 from A. Identities between Ch1 and Rat2 are shown in boldface type.

Figure 18 shows immunoprecipitation and immunoblotting of $PP1_M$ in extracts from chicken gizzard myofibrils.

A. Antibodies specific for the M_{110} and/or M_{21} subunits immunoprecipitate most of the myosin P-light chain phosphatase activity in myofibrillar extracts. $PP1_M$ was immunoprecipitated with either control IgG, antibody raised against the $PP1_M$ holoenzyme, antibody specific for the M_{110} subunit or antibody specific for the M_{21} subunit, as described under Methods in Example 3. The figure shows activity present in the supernatant (S, open bars) or pellet (P, filled bars) as a percentage of that measured before centrifugation. The results shown are the average ($\pm$ S.E.M.) for three separate experiments each assayed in duplicate. B, The M_{110} and M_{21} subunits are present in similar molar proportions in myofibrillar extracts and in purified $PP1_M$. 10 ng (track 1) or 3 ng (track 3) of purified $PP1_M$ or 12 μg (track 2) or 3.6 μg (track 4) of myofibrillar extract was electrophoresed on a 12% SDS/polyacrylamide gel, transferred to nitrocellulose and immunoblotted with mixed affinity-purified antibodies to the M_{110} and M_{21} subunits as in [22]. The positions of the two subunits are marked. The results indicate that $PP1_M$ comprises about 0.1% of the myofibrillar protein.

Figure 19 shows the identification of the region on the M_{110} subunit that

interacts with the M_{21} subunit.

A) $PP1_M$ 5 μg (track 1), 10 μg bacterial extract containing M_{110}-(R714-I1004) (track 2), MBP-M_{110}-(R714-I1004) 1 μg (track 3), MBP-M_{110}-(R714-L934) 1 μg (track 4), MBP-M_{110}-(K933-I1004) 1 μg (track 5), MBP 1μg (track 6), M_{110}-(M1-E309) 2 μg (lane 7) and M_{110}-(M1-S477) 2 μg (track 8) were run on a 12% SDS/polyacrylamide gel and stained with Coomassie Blue. **B)** same as **A)** except that 10-fold less protein was electrophoresed and after transfer to nitrocellulose the proteins were probed with digoxigenin-labelled M_{21} subunit (0.2 μg/ml). **C)** same as **B)** except that, after electrophoresis, the proteins were transferred to nitrocellulose and probed with digoxigenin-labelled M_{21}-(M1-L146) (0.2 μg/ml).

Figure 20 shows the identification of the region of the M_{21} subunit involved in interaction with the M_{110} subunit and in dimerization.

A) GST-M_{21} 5 μg (track 1), M_{21} 5 μg (track 2), M_{21}-(M1-L146) 5 μg (track 3), M_{21}-(M1-E110) 20 μg (track 4) and M_{21}-(E110-K186) 5 μg (track 5) were run on 16.5% polyacrylamide gels and stained with Coomassie Blue. The marker proteins ovalbumin (43 kDa) and carbonic anhydrase (29 kDa) are indicated. **B)** GST-M_{21} 0.5 μg (track 1), M_{21} 0.5 μg (track 2), M_{21}-(M1-L146) 0.5 μg (track 3), M_{21}-(M1-E110) 5 μg (track 4) and M_{21}-(E110-K186) 5 μg (track 5) were electrophoresed as in **A)** and after transfer to nitrocellulose the blots were probed with digoxigenin-labelled MBP-M_{110}-(K933-I1004) (0.2 μg/ml). **C)** same as **B)** except that, after electrophoresis, the proteins were transferred to nitrocellulose and probed with digoxigenin-labelled M_{21} subunit (0.2 μg/ml).

Figure 21 shows that the M_{21} subunit and M_{21}-(M1-L146) interact with the M_{110} subunit and themselves, but not with PP1.

$PP1_M$ (0.5 μg) was electrophoresed on a 12% SDS/polyacrylamide gel, transferred to nitrocellulose and probed with digoxigenin-labelled M_{21} subunit (0.2 μg/ml) (track 1) or digoxigenin-labelled M_{21}-(M1-L146) (0.2 μg/ml) (track 2). The positions of the M_{110} subunit, the M_{21} subunit and PP1c are marked.

Figure 22 shows that removal of the M_{21} subunit from smooth muscle $PP1_M$ does not prevent it from being pelleted with myosin.

The PP1 catalytic subunit (PP1c), $PP1_M$, or $PP1_M$ lacking the M_{21} subunit, $PP1_M(\Delta M_{21})$, each at 30 nM, were incubated for 15 min at 0°C with 1 μM myosin and centrifuged (see Methods of Example 3). The figure shows the myosin P-light chain phosphatase activity present in the supernatant (S, open bars) or pellet (P, filled bars) as a percentage of that measured before centrifugation. The results shown are the average ($\pm$ S.E.M.) for three separate experiments each assayed in duplicate.

Figure 23 shows the identification of a region of the M_{110} subunit which binds to myosin.

(A); $PP1_M$, M_{110}-(M1-S477) and GST-M_{110}-(M377-K976), each at 30 nM were incubated for 15 min at 0°C with 1 μM myosin and centrifuged. The supernatants (S), resuspended pellets (P) and the suspension before centrifugation (T, total) were electrophoresed on 12% SDS/polyacrylamide gels, transferred to nitrocellulose and immunoblotted with antibodies raised against the $PP1_M$ holoenzyme. No protein was pelleted in the absence of myosin (not shown). The positions of the marker proteins myosin heavy chain (200 kDa), glycogen phosphorylase (97 kDa), bovine serum albumin (66 kDa), ovalbumin (43 kDa), carbonic anhydrase (29 kDa) and soybean trypsin inhibitor (20 kDa) are indicated. (B) The experiments were carried out as in (A), except that the M_{110} fragments and M_{21} subunit were used at 100 nM, the 8.5 kDa

M_{110}-(K933-I1004) fragment was electrophoresed on a 16.5% polyacrylamide gel and immunoblotting was carried out with affinity purified antibodies (see Methods). A small amount of M_{110}-(R714-I1004) pelleted in the absence of myosin. This was probably due to aggregation in the bacterial extract since this did not happen when it was complexed to the M_{21} subunit (data not shown). No other protein was pelleted in the absence of myosin.

Figure 24 shows that the isolated M_{21} subunit binds to myosin.

(A); Myosin (1 μM) was mixed with 50 μM, 20 μM or 10 μM M_{21} subunit to give the molar ratios M_{21}:myosin dimer indicated. After 15 min at 0°C, the solutions were centrifuged and the supernatants (S), resuspended pellets (P) and the suspension before centrifugation (T, total) were electrophoresed on 12% SDS/polyacrylamide gels and stained with Coomassie blue. The positions of the myosin heavy chain (MHC) and the M_{21} subunit are indicated. The myosin light chains migrate faster than the M_{21} subunit and are not visible at these loadings.

(B); Myosin (track A) was purified from chicken gizzard, and the myosin "rod" domain (track B) and light meromyosin (track C) produced by digestion of myosin with papain and chymotrypsin, respectively. These three proteins, all at 1 μM, were then mixed with M_{21} subunit (track D) to give a molar ratio M_{21}:myosin dimer of 10:1 and, after 15 min at 0°C, the solutions were centrifuged and the supernatants (S), resuspended pellets (P) and the suspension before centrifugation (T, total) were electrophoresed on 12% SDS/polyacrylamide gels and stained with Coomassie blue. The slightly faster migrating band in the M_{21} subunit preparation was shown by amino acid sequencing to be N-terminally truncated commencing at residue 16. **(C)**; same as **(B)**, except that M_{21}-(M1-L146) (track D) replaced the M_{21} subunit.

Figure 25 gives a schematic representation of the regions on the M_{110} subunit from chicken gizzard that interact with PP1c, myosin and the M_{21} subunit.

PP1c binds to the KVKF (SEQ ID No 5) motif between residue 35 and 38, just N-terminal to the seven ankyrin repeats (hatched vertical lines) that suppress the dephosphorylation of substrates other than myosin. Residues 1-38 of the M_{110} subunit enhance the dephosphorylation of myosin. The M_{21} subunit binds to the C-terminal 72 residues of the M_{110} subunit which are 43% identical in amino acid sequence to residues 87-161 of the M_{21} subunit. The dephosphorylated form of myosin binds to M_{110}-(R714-I1004) but not to M_{110}-(K933-I1004), suggesting that myosin binds N-terminal to the M_{21} subunit.

<u>**Example 1: Identification of protein phosphatase 1-binding domains on the glycogen and myofibrillar targeting subunits**</u>

MATERIALS AND METHODS

Materials.

The myosin-associated form of PP1 ($PP1_M$) was from chicken gizzard [9] and the glycogen-associated form of PP1 ($PP1_G$) from rabbit skeletal muscle [21]. The β isoform of PP1c was released from $PP1_G$ by incubation for 2 hours in 2M LiBr, then purified by gel-filtration on a 30 x 1 cm column of Superose 12 (Pharmacia, Milton Keynes, U.K.) in the presence of 0.5M LiBr. Glycogen protein particles from rat liver [22] were used as the source of hepatic $PP1_G$. Digoxygenin-labelled PP1c (γ_1-isoform, hereafter termed PP1) was prepared as in [9]. G_L was expressed in *E. coli* as a glutathione-S-transferase (GST) fusion protein [7], termed GST-G_L. The catalytic subunit of PP2A from bovine heart (PP2AC) was provided by Dr R. MacKintosh in this Unit. The phosphorylatable myosin light chain (MLC_{20}) and heavy meromyosin from chicken gizzard were a gift from Dr M. Ikebe (Case Western Reserve

University, Cleveland, USA). Thrombin and benzamidine-Agarose were purchased from Sigma (Poole, UK).

Peptide synthesis.

Peptides were synthesised on an Applied Biosystems 430A peptide synthesiser and their purity and concentration established by high performance liquid chromatography, mass spectrometry and amino acid analysis. The sequence of rabbit G_M-(G63-T93) is GRRVSFADNFGFNLVSVKEFDTWELPSVSTT (SEQ ID No 6) and the sequence of M_{110}-(M1-F38) is MKMADAKQKRNEQLKRWIGSETDLEPPVVKRQKTKVKF (SEQ ID No 7). The peptide G_M-(G63-T93) was cleaved with Lys-C endoproteinase (Boehringer) and the peptide G_M-(E81-T93) thus generated was purified on a C_{18} column. The peptides G_M-(G63-K80) and G_M-(G63-N75), were synthesised, and the latter phosphorylated at Ser67 with the catalytic subunit of cyclic AMP-dependent protein kinase (PKA), then bound to a 1 ml C_{18} column equilibrated in 0.1% (v/v) trifluoroacetic acid, washed with 0.1% trifluoroacetic acid to remove excess ATP, eluted with 0.1% trifluoroacetic acid containing 70% acetonitrile, dried and dissolved in water. The peptide G_M-(S40-Y55) was a gift from Dr Bruce Kemp (St Vincent's Institute, Australia).

Preparation of phosphorylated proteins and phosphatase assays.

^{32}P-labelled rabbit skeletal muscle phosphorylase a (containing 1.0 mol phosphate per mol subunit) was prepared by phosphorylation with phosphorylase kinase [23], ^{32}P-labelled rabbit skeletal muscle glycogen synthase (containing 1.5 mol/mol subunit in the sites 3 region) was prepared by phosphorylation with glycogen synthase kinase-3 [24]), ^{32}P-labelled chicken gizzard MLC_{20} and ^{32}P-labelled chicken gizzard heavy meromyosin (containing 1.0 mol phosphate per mol subunit) were prepared by phosphorylation with smooth muscle myosin light chain kinase [9]. The dephosphorylation of

phosphorylase a (10 μM), glycogen synthase (1 μM) and MLC_{20} (1 μM) and heavy meromyosin (1 μM) was carried out as in [24]. One unit of activity (U) was that amount which released 1 mole of phosphate in one minute.

Construction of vectors for the expression of N-terminal fragments of the G_M subunit as glutathione-S-transferase (GST) fusion proteins in E. coli.

G_M-(E2-R575) was produced by inserting a SmaI-SmaI restriction fragment, encoding amino acids 2-575 of human G_M, from clone H1G11 [5] into the SmaI site of pGEX-KG (Pharmacia, Milton Keynes, U.K.). This resulted in the addition after residues 2-575 of amino acids EFPVVVVEF (SEQ ID No 8) before the stop codon. G_M-(E2-P243) was made by deleting an NcoI-HindIII fragment of the G_M-(E2-R575) construct, resulting in termination after residue 243. G_M-(E2-D118), encoding amino acids 2-118, with a C-terminal addition of QLNSS was produced by deleting a BglII-HindIII fragment of the G_M-(E2-R575) construct. G_M-(H100-P350) encoding amino acids 100-350 was made by inserting an EcoRI-HindIII digested PCR fragment prepared using primers

5′ GCCGAATTCACACAGAAGAATATGTTTTAGCC 3′ (SEQ ID No 9) and

5′ GCCGAAGCTTATGGAAAATTGACTGGATCTGTTG 3′ (SEQ ID No 10)

into the same sites of pGEX-KG. Restriction sites in the primers are underlined.

Construction of vectors for the expression of the chicken gizzard M_{21} subunit in E. coli.

The entire coding region (M1-K186) of the M_{21} subunit [10] was amplified by PCR using primers

5′ CGCGCATATGTCGTCGCTGTTCACCAGG 3′ (SEQ ID No 11) and

5′ GGCGGATCCCTACTTGGAGAGTTTGC 3′ (SEQ ID No 12), containing

restriction sites NdeI and BamH1 (underlined). After cleavage with the restriction enzymes, the PCR fragment was cloned into the same sites of the bacterial expression vector pT7-7.

Production of fragments of the chicken gizzard and rat aorta M_{110} subunits.

The C-terminal 291 residues M_{110}-(R714-I1004) of the chicken gizzard M_{110} subunit were amplified by PCR using a primer 5′ AGGAAGAATTCGTTCCACACGAAC 3′ (SEQ ID No 13) containing an EcoRI restriction site (underlined) and a KS primer in the Bluescript vector of the cDNA clone [10]. The EcoRI digested PCR fragment was subcloned into the same site of pT7-7.

Rat aorta M_{110} fragments were produced as GST-fusion proteins. M_{110}-(M1-A150) was amplified by PCR using primers A (5′ CCTAG<u>CCCGGG</u>GATGAAGATGGCGGAC 3′) (SEQ ID No 14) and B (5′ GCGG<u>AAGCTT</u>ATGCTTCCTCCTCTGCAATATC 3′) (SEQ ID No 15), containing SmaI and HindIII restriction sites (underlined) and the SmaI-HindIII digested PCR fragment subcloned into the same sites of pGEX-KG. M_{110}-(M1-E309) was produced by subcloning a SmaI-HindIII digested PCR fragment amplified using primers A and C (5′ CTAGAAGCTTCCATATTTGCTGTTGATTCAATC 3′) (SEQ ID No 16) into the same sites of pGEX-KG. This resulted in one amino acid (A) being added after E309. M_{110}-(D39-E309) was produced by subcloning a SmaI-HindIII digested PCR fragment amplified using primers D (5′ CCTAGCCCGGGGGACGATGGCGCCGTCTTCC 3′) (SEQ ID No 17) and C into the same sites of pGEX-KG. An M_{110}-(L24-K976) was prepared by inserting a XhoI-XhoI restriction fragment of the entire M_{110} cDNA in Bluescript into XhoI site of pGEX-KG, and M_{110}-(L24-Y496) expressed by deleting a NdeI-NdeI fragment of the L24-K976 construct and filling the

overhanging ends before ligating them. This resulted in the addition after Y496 of amino acids MVAD (SEQ ID No 18) before the stop codon. The sequence of all subclones produced after PCR amplification were verified using an Applied Biosystems 373A automated DNA sequencer and Taq dye terminator cycle sequencing according to the manufacturer's instructions.

Expression of proteins in E.coli.

All constructs were expressed in *E. coli* strain BL21(DE3)plysS. Cultures were grown at 37°C in Luria-Bertani medium in the presence of 100 μg/ml ampicillin and 30 μg/ml chloramphenicol to an A600 of 0.4-0.6, and induced with 50 μg/ml isopropylthiogalactoside for 8 hours at 25°C or overnight at ambient temperature. After centrifugation for 10 minutes at 7000 x g (4°C), cells from one litre of culture were resuspended in 20 ml of 50 mM Tris-HCl pH 8.0, 0.1 M NaCl, 1 mM EDTA, 0.1% (by vol) 2-mercaptoethanol, 0.2 mM phenylmethylsulphonylfluoride ($PhMeSO_2F$), 1 mM benzamidine (buffer A) and frozen at -80°C. After thawing, sodium deoxycholate (1 mg/ml), 8 mM MgSO4 and 10 g/ml DNAase I were added, the extract incubated until it was no longer viscous, then made 6 mM in EDTA, 1 mM in benzamidine and 0.2 mM in $PhMeSO_2F$ and centrifuged for 10 minutes at 10,000 x g. The soluble GST-fusion proteins were then purified from the supernatant by affinity chromatography on glutathione-Sepharose (Pharmacia).

The M_{21} subunit and M_{110}-(R714-I1004) C-terminal fragment from chicken gizzard M_{110} subunit, which were used for affinity purification of the anti-M_{21} and anti-M_{110} antibodies (see below) were obtained in inclusion bodies and therefore recovered in the pellets after centrifuging *E. coli* extracts at 10,000 x g. M_{110}-(R714-I1004) was solubilised by resuspension in Buffer A containing 0.5% (by mass) Triton X-100 and was >95% pure. The M_{21} subunit was not solubilised by this procedure but, after washing the pellets in 0.5% Triton

X-100, was dissolved by sonication in 0.5% trifluoroacetic acid; its purity was about 20%.

M_{110} GST-fusion proteins (1-9 mg/ml in 50 mM Tris/HCl, 2.5 mM CaCl2, 150 mM NaCl and 0.1% (by vol) 2-mercaptoethanol) were cleaved by incubation for 20 minutes at 30°C with 20 μg/ml thrombin. Benzamidine-Agarose (0.2 ml) was added and, after incubation (with rotation) for 30 minutes at ambient temperature, the benzamidine-Agarose containing the attached thrombin was removed, and the supernatant dialysed against 50 mM Tris-HCl pH 7.5, 0.1 mM EGTA, 0.1% (by vol) 2-mercaptoethanol, 10% glycerol and stored in aliquots at -80°C. After cleavage with thrombin, all fragments of the M_{110} subunit, except M_{110}-(L24-Y496), commenced with the sequence GSPG (SEQ ID No 19) before the initiating residue of the GST-fusion proteins. The M_{110}-(24-Y496) was preceded by the sequence GSPGISGGGGGILDSMGR (SEQ ID No 20).

Production of antibodies that recognise the M_{110} and M_{21} subunits of chicken gizzard $PP1_M$.

Polyclonal sheep antibodies to the $PP1_M$ holoenzyme were raised in the Scottish Antibody Production Unit (Carluke, Ayrshire, U.K.). Antibodies which recognise the M_{110} subunit specifically were obtained by passing the antiserum down a 4 ml affinity column comprising 40 mg of M_{110}-(R714-I1004) coupled covalently to 1g of dried CNBr-activated Sepharose 4B (Sigma). After washing with 10 column volumes of 50 mM Tris/HCl pH 7.5, 1% (by mass) Triton X-100, 0.1 mM EGTA, 0.1% (by vol) 2-mercaptoethanol (Buffer B) plus 0.5 M NaCl, followed by 10 volumes of Buffer B plus 1 M LiBr, the anti-M_{110} antibody was eluted with 50 mM glycine pH 2.0, neutralised immediately with 1 M Tris/HCl pH 8.0 and stored in aliquots at -80°C. Antibodies which recognise the M_{21} subunit specifically were obtained in an

identical manner, except that the affinity column comprised about 40 mg of the expressed chicken gizzard M_{21} subunit coupled to 6 g (dry weight) of CNBr-activated Sepharose.

Removal of the M_{21} subunit from $PP1_M$.

$PP1_M$ (0.01 ml, 0.4U/ml) was dissociated by incubation for 30 minutes with 500 μM arachidonic acid [25] and then for 30 minutes with 0.08 ml of packed Protein G-Sepharose coupled to 0.08 mg of affinity purified anti-M_{21} antibody. The Protein G-Sepharose was pelleted, and the supernatant diluted at least 15-fold to allow the M_{110} subunit and PP1c to recombine. The M_{110}-PP1c complex was further purified by gel filtration on Superose 12 (30 x 1 cm) to ensure complete removal of any free PP1c.

RESULTS.

Identification of a PP1c-interaction domain on the G_M-subunit of $PP1_{GM}$.

The amino acid sequence of rat hepatic G_L is 23% identical (39% similar) to residues 1-286 of G_M from human skeletal muscle [7]. There is no homology over the first 63 residues but identity is >40% over the regions 63-86, 144-166 and 186-227 of G_M suggesting that one or more of these sequences comprise a PP1-binding domain. Fusion proteins in which GST was linked to fragments of G_M were therefore tested for their ability to bind to PP1c. GST-G_M-(E2-D118) (Fig 1) and GST-G_M-(E2-P243) (data not shown), but not GST-G_M- (H100-P350) or GST itself (Fig 1) interacted with PP1 in Far Western experiments, indicating that the first 118 residues of G_M contain a PP1c-binding domain. Moreover, a proteolytic fragment derived from GST-G_M-(E2-D118) whose molecular mass was 5 kDa less than GST-G_M-(E2-D118), but not a proteolytic fragment that was 6 kDa smaller, also interacted with PP1c (Fig 1). Taken together, the observations suggested that the region comprising residues 63-86 was likely to bind to PP1c. We

therefore synthesised G_M-(G63-T93) and examined its effect on the enzymatic properties of $PP1_{GL}$, the form of PP1 associated with rat hepatic protein-glycogen particles.

The interaction of PP1c with G_L suppresses the dephosphorylation of muscle glycogen phosphorylase by 80% and enhances the dephosphorylation of muscle glycogen synthase by 2-3 fold [21, 26]. Disruption of the characteristic properties of hepatic $PP1_{GL}$ can therefore be monitored very simply by changes in its specificity. G_M-(G63-T93) induced a sixfold increase in the phosphorylase phosphatase activity of $PP1_{GL}$, the concentrations required for 50% activation being 30 nM (Fig 2). G_M-(G63-T93) also prevented bacterially expressed GST-G_L from suppressing the phosphorylase phosphatase activity of PP1c (data not shown). However, G_M-(G63-T93) had no effect on the glycogen synthase phosphatase activity of $PP1_{GL}$, nor was there any alteration of the other characteristic properties of $PP1_{GL}$, namely allosteric inhibition of the glycogen synthase phosphatase activity by phosphorylase a and binding to glycogen (data not shown). Thus the interaction of G_M-(G63-T93) with $PP1_{GL}$ does not displace G_L from PP1c.

G_M-(G63-T93) also increased the phosphorylase phosphatase activity of PP1c, indicating that it binds to PP1c, rather than to G_L. However, the maximal stimulation was only 37 + 1.4% (SEM for three experiments), establishing that far greater activation of $PP1_{GL}$ is explained by the ability of G_M-(G63-T93) to overcome the suppressive effect of G_L on the phosphorylase phosphatase activity of PP1c. Several other peptides, including a 32 residue peptide related to the C-terminus of ribosomal protein S6([G245,G246]S6[218-249]), G_M-(S40-Y55) and G_M-(E81-T93) (data not shown), had no effect on the phosphorylase phosphatase activity of $PP1_{GL}$ or PP1c at concentrations up to 10 μM.

The peptides G_M-(G63-K80) and G_M-(G63-N75) also increased the phosphorylase phosphatase activity of $PP1_{GL}$, but were less effective than G_M-(G63-T93) and higher concentrations were needed (Fig 2). G_M-(G63-K80) and G_M-(G63-N75) did not increase the phosphorylase phosphatase activity of PP1c significantly at concentrations up to 10 μM (data not shown). The phosphorylation of G_M at Ser67 by cyclic AMP-dependent protein kinase (PKA) triggers the dissociation of PP1 from G_M *in vitro* and *in vivo* [18] and phosphorylation of the peptide G_M-(G63-N75) at Ser67 prevented it from increasing the phosphorylase phosphatase activity of $PP1_{GL}$ (Fig 2A). The increase in phosphorylase phosphatase activity observed at the highest phosphopeptide concentrations (10 μM) may be explained by trace contamination ($<10\%$) with dephosphopeptide, resulting either from incomplete phosphorylation of Ser67 or slight dephosphorylation during the assay.

Identification of a PP1-interaction domain on the M_{110} subunit.

Antibodies were prepared that recognised either the M_{110} or M_{21} subunits of the myosin-associated form of PP1 ($PP1_M$) from chicken gizzard (Fig 3A). Removal of the M_{21} subunit using the M_{21}-specific antibody (Fig 3B and see Methods) did not affect the activity of $PP1_M$ towards MLC_{20} or phosphorylase, the MLC_{20} phosphatase:phosphorylase phosphatase activity ratio (0.95 ± 0.03) remaining 15-fold higher than PP1c (Fig 3B). The M_{21} subunit bound to M_{110}, but had no effect on the MLC_{20} phosphatase or phosphorylase phosphatase activity of PP1c and did not bind to PP1c (D. Johnson unpublished). Thus M_{110} is solely responsible for enhancing the dephosphorylation of MLC_{20} and suppressing the dephosphorylation of glycogen phosphorylase by PP1c [9].

In order to identify which region(s) of M_{110} modulates the specificity of PP1c, fusion proteins were constructed consisting of glutathione S-transferase (GST) followed by fragments of the M_{110} subunit. After expression in *E. coli* and

purification by affinity chromatography on glutathione-Sepharose, the fusion proteins were cleaved with thrombin to release GST from fragments of the M_{110} subunit (Fig 4 and see Methods). M_{110}-(M1-E309), which contains seven 33 residue ankyrin repeats located between residues 39-296, modified the specificity of PP1c in a similar manner to M_{110} itself, increasing activity towards MLC_{20} about 3-fold (Fig 5A) and suppressing activity towards glycogen phosphorylase by about 80% (Fig 5B). The concentration of M_{110}-(M1- E309) required to activate the MLC_{20} phosphatase activity maximally (0.1 nM) was similar to the PP1c concentration in the assay, indicating an extremely high affinity for PP1c. M_{110}-(M1-A150) modified the specificity of PP1 similarly, but 10-fold higher concentrations were needed compared to M_{110}-(M1-E309) (Figs 5C and 5D).

If the GST tags were not cleaved with thrombin, a 10-fold higher concentration of M_{110}-(M1-E309) was needed to modulate the substrate specificity of PP1c, while M_{110}-(M1-A150) was unable to stimulate the MLC_{20} phosphatase activity of PP1c at all (data not shown). GST itself did not interact with PP1c (Fig 1), had no effect on either the MLC_{20} phosphatase or phosphorylase phosphatase activity of PP1c (data not shown), and therefore was not removed from the solution after cleavage of the fusion proteins with thrombin.

In contrast to M_{110}-(M1-E309), M_{110}-(D39-E309) failed to stimulate the MLC_{20} phosphatase activity of PP1c, or to inhibit its phosphorylase phosphatase activity (Figs 5A and 5B), suggesting that the extreme N-terminus of the M_{110} subunit (i.e. before the start of the ankyrin repeats) might be important in modulating the specificity of PP1c. The peptide M_{110}-(M1-F38) was therefore synthesized and found to stimulate the MLC_{20} phosphatase activity of PP1c to the same extent as M_{110}-(M1-E309), although the concentration required for half maximal activation (10 nM) was at least 100-fold higher (Fig 5A). M_{110}-(M1-F38) stimulated the dephosphorylation of heavy meromyosin in a

similar manner to the dephosphorylation of MLC_{20} (data not shown). However, like M_{110}-(D39-E309), M_{110}-(M1-F38) did not inhibit the phosphorylase phosphatase activity of PP1c (Fig 5B). These observations suggested that residues beyond 38 were needed to suppress phosphorylase phosphatase activity. Consistent with this, M_{110}-(L24-Y496) was less effective than M_{110}-(M1-A150) or M_{110}-(M1-E309) in stimulating the MLC_{20} phosphatase activity of PP1c, but inhibited the phosphorylase phosphatase activity of PP1c in a similar manner to M_{110}-(M1-A150) (Figs 5C and 5D).

Although M_{110}-(D39-E309) and M_{110}-(M1-F38) had no effect on the phosphorylase phosphatase activity of PP1c when each peptide was included individually in the assays at concentrations up to 1 μM (Fig 5), a 39 $\pm$ 2% inhibition (SEM n=4) was observed when both peptides were both present at 1 μM. Surprisingly, M_{110}-(D39-E309) prevented (IC50 = 0.1 M) M_{110}-(M1-F38) from stimulating the MLC_{20} phosphatase activity of PP1c (data not shown). Thus M_{110}-(D39-E309) plus M_{110}-(M1-F38) do not faithfully mimic the effect of M_{110}-(M1-E309).

We have reported previously that the M_{110}/M_{21} complex suppresses the dephosphorylation of glycogen synthase by PP1c [9] and, consistent with this finding, the dephosphorylation of glycogen synthase was also inhibited by M_{110}-(M1-E309) (Fig 6B). However, the dephosphorylation of glycogen synthase was greatly enhanced by M_{110}-(M1-F38) (Fig 6A).

The binding of G_M and the M_{110} subunit to PP1c is mutually exclusive.

In order to investigate whether G_M binds to the same region of PP1c as M_{110}, we next examined the effect of G_M-(G63-T93) on the properties of $PP1_M$. G_M-(G63-T93) at 10 μM increased the phosphorylase phosphatase activity of $PP1_M$ by about 7-fold and suppressed its MLC_{20} phosphatase activity by 60-65%

(Fig 7A), indicating that the distinctive properties of $PP1_M$ had been disrupted. Gel-filtration experiments confirmed that G_M-(G63-T93) had displaced the M_{110} subunit from $PP1_M$, dissociating it to PP1c (Figs 7B and 7C). G_M-(G63-T93) also prevented M_{110}-(M1-F38) or M_{110}-(M1-E309) from stimulating the MLC_{20} phosphatase activity of PP1c (Fig 8A), and prevented M_{110}-(M1-E309) from suppressing the phosphorylase phosphatase activity of PP1c (Fig 8B).

Conversely, the presence of 10 μM M_{110}-(M1-F38) increased the phosphorylase phosphatase activity of $PP1_{GL}$ by 3.5- fold. This resulted from the partial dissociation to PP1c, because the enhanced phosphorylase phosphatase activity was not associated with glycogen, but recovered in the supernatant after centrifugation of the glycogen-protein particles (not shown).

DISCUSSION.

We have identified a region on G_M that binds to PP1c (Fig 9). The peptides G_M-(G63-T93), G_M-(G63-K80) and G_M-(G63-N75) all prevented G_L from suppressing the dephosphorylation of glycogen phosphorylase by PP1c and two lines of evidence indicate that these peptides interact with PP1c and not with G_L.

Firstly, the PP1c-catalysed dephosphorylation of glycogen phosphorylase is stimulated slightly by G_M-(G63-T93).

Secondly, PP1c crystallises in the presence of G_M-(G63-K80) or G_M-(G63-N75) in a different form than is observed in the absence of these peptides. PKA phosphorylates G_M at Ser67 and the introduction of a negative charge directly into the PP1c-binding domain explains why phosphorylation of Ser67 triggers the dissociation of G_M from PP1c [18]. Phosphorylation of G_M-(G63-N75) at Ser67 also prevented this peptide from interacting with PP1 in the $PP1_{GL}$

complex (Fig 2).

Although G_M-(G63-T93) prevented G_L from suppressing the dephosphorylation of glycogen phosphorylase by PP1c, it did not dissociate G_L from PP1c, nor did it affect the other characteristic properties of $PP1_{GL}$. Moreover, unlike G_L, G_M-(G63-T93) did not itself suppress the phosphorylase phosphatase activity of PP1c, but actually enhanced it slightly. These observations demonstrate that another region(s) on G_L must interact with PP1c and that this other region(s) may play an important role in modulating the substrate specificity of PP1c. The presence of a second PP1c binding site in G_M/G_L would be somewhat analogous to the situation found in inhibitor-1 and DARPP which also contain two PP1-binding sites, high (nM) affinity binding being generated by the conjugation of two low affinity binding sites that, individually, only interact with PP1 at μM concentrations [28]. The second PP1c-binding site on G_M/G_L might correspond to one of the other regions where G_M and G_L show >40% identity (residues 144-166 and 186-227 of human G_M). Although G_M-(H100-P350) was not recognised by PP1c in Far Western experiments (Fig 1) this result is not definitive because G_M-(H100-P350) may only interact with PP1c weakly. Alternatively, G_M-(H100-P350) might not fold correctly or fail to renature after SDS/polyacrylamide gel electrophoresis.

However, it is also possible that residues 144-166 and 186-227 of G_M do not represent part of the second PP1c-binding domain, but part of the glycogen-binding domain. In this connection it should be recalled that residues 144-166 and 186-227 are the regions showing greatest similarity (25% identity) to GAC1, which appears to be a homologue of G_M/G_L in budding yeast [7, 27, 28]. Curiously, GAC1 does not contain a region homologous to residues 63-93 of G_M/G_L. It would clearly be of interest to compare the effect of GAC1 on the enzymatic properties of PP1c with those of G_M and G_L.

We have also identified a region on the M_{110} subunit that binds to PP1c. An N-terminal fragment, M100-(M1-E309), enhanced the PP1c-catalysed dephosphorylation of MLC_{20} and suppressed the dephosphorylation of glycogen phosphorylase in a similar manner to M_{110} itself (Fig 5). However, unlike M_{110}, this fragment does not bind to myosin. Thus the region which enhances the dephosphorylation of MLC_{20} is distinct from the myosin-binding domain.

The fragment M_{110}-(M1-E309) contains seven ankyrin repeats lying between residues 39 and 296. However, M_{110}-(D39-E309) was ineffective as an activator of the MLC_{20} phosphatase activity of PP1c or as an inhibitor of the phosphorylase phosphatase activity, and this led to the finding that a peptide comprising the N-terminal 38 residues of the M_{110} subunit enhances the dephosphorylation of MLC_{20} to the same extent as M_{110}-(M1-E309), although with lower potency. However, M_{110}-(M1-F38) did not inhibit the dephosphorylation of glycogen phosphorylase by PP1c suggesting that residues beyond 38 are required to suppress this activity. This view was reinforced by the finding that, although neither M_{110}-(M1-F38) nor M_{110}-(D39-E309) inhibited the phosphorylase phosphatase activity of PP1c when present individually, inhibition was observed in the presence of both peptides. Moreover M_{110}-(D39-E309) actually prevented M_{110}-(M1-F38) from stimulating the dephosphorylation of MLC_{20}.

These observations suggest that M_{110}-(D39-E309) can bind to M_{110}-(M1-F38) and/or PP1c. An interaction with PP1c seems likely because it has been found that M_{110}-(D39-E309) can enhance the phosphorylase activity of $PP1_{GL}$. The presence of a second PP1-binding site in the ankyrin-repeat domain of the M_{110} subunit is also supported by the observation that higher concentrations of M_{110}-(M1-A150) and M_{110}-(M1-E309) are needed to inhibit the phosphorylase phosphatase activity of PP1c than are required to stimulate its MLC_{20} phosphatase activity (see Fig 5). The presence of at least two PP1-binding sites

may explain why the M_{110} subunit and PP1c interact at picomolar concentrations. The ankyrin repeat domain might suppress the dephosphorylation of some substrates (such as glycogen phosphorylase) by a steric mechanism, preventing them from gaining easy access to the catalytic centre. This scenario could explain why the dephosphorylation of glycogen synthase is greatly enhanced by M_{110}-(M1-F38) yet suppressed by M_{110}-(M1-E309) (Fig 6).

G_M-(G63-T93) abolished the distinctive properties of $PP1_M$ (Fig 7A), prevented M_{110}-(M1-F38) or M_{110}-(M1-E309) from modulating the substrate specificity of PP1c (Fig 8) and displaced the M_{110} subunit from $PP1_M$ (Fig 7B). In addition, the peptide M_{110}-(M1-F38), was capable of displacing G_L from $PP1_{GL}$. These findings indicate that the binding site(s) on PP1c for G_M and the M_{110} subunit are likely to overlap, explaining why different forms of PP1 contain a single PP1-targeting subunit. The three-dimensional structure of PP1c isoforms have recently been solved to high resolution [29,30], and PP1c crystallises in different forms in the presence of G_M-(G63-N75) or G_M-(G63-K80) or M_{110}-(M1-F38) than in the absence of these peptides.

Consistent with the results presented here, Gailly *et al* [31] have recently shown that M_{110}-(M1-F38) or M_{110}(M1-E309) enhance the ability of PP1c to stimulate the relaxation of microcystin-contracted permeabilised portal vein, while G_M-(G63-T93) inhibits the ability of $PP1_M$ to induce the relaxation of this smooth muscle. G_M-(G63-T93) also slowed the relaxation of permeabilised femoral artery, indicating that it competes with the endogenous M_{110} subunit for PP1c [31]. Thus the PP1c-binding peptides described constitute useful pharmacological agents with which to explore the role and regulate the activity of PP1 in cell regulation.

Example 2: Structural basis for the recognition of regulatory subunits by the catalytic subunit of protein phosphatase 1

MATERIALS AND METHODS

Crystallisation and Data Collection

The catalytic subunit of PP1 1 was overproduced in *Escherischia coli* and purified as described previously (Alessi *et al.*, 1993; Barford and Keller, 1994). The G_M[G63-N75] peptide, variants of this peptide in which Val 66' or Phe 68' were changed to Phe, and the peptides M_{110}[1-38] and M_{110}[1-35] were synthesised on an Applied Biosystems 430A peptide synthesiser and purified by chromatography on a C18 column (Johnson *et al.*, 1996) by Mr F.B. Caudwell at Dundee. A three-fold molar excess of G_M[G63-N75] was added to the protein solution (8 mg/ml), which had been previously dialysed against 10 mM Tris-HC1 (pH 7.8), 0.3 M NaCl, 0.4 mM $MnCl_2$ and 2 mM DTT. The complex was crystallised at 20°C using the hanging drop vapour diffusion method, by mixing 2 ml of the protein-peptide solution and 2 ml of the precipitant solution containing 2.0 M ammonium sulphate, 2% (w/v) polyethylene glycol 400,100 mM HEPES (pH 7.5) and 2 mM DTT. These conditions are very much in contrast to the relatively low ionic strength conditions from which the monoclinic PP1c crystals grew (Barford and Keller, 1994; Egloff *et al.*, 1995). Crystals appeared after 3 months as a cluster. Individual crystals removed from the cluster had dimensions of ~25 μm x 25 μm x 5 μm. Crystals were frozen in a 100 K nitrogen gas stream and stored. Prior to freezing, crystals were incubated in a cryoprotectant solution consisting of an equilibration buffer; 2.0 M ammonium sulphate, 2% (w/v) PEG 400, 100 mM HEPES (pH 7.5) with increasing amounts of glycerol in steps of 7%, 15%, 22% and 30% (v/v).

A partial data set to 3.0 Å was collected on Beam Line PX 9.6, SRS,

Daresbury, using a 30 cm diameter Mar Research image plate system. Data were processed and scaled using DENZO and SCALEPACK (Otwinowski, 1993). The crystal system is tetragonal with point group symmetry P422 and unit cell dimensions a = b = 62.50Å, c = 361.30Å. Systematic absences indicate a 21 screw axis along b. The Matthews coefficient was 2.38 $Å_3$ per Dalton, assuming 2 molecules per asymmetric unit. A second data-set was collected on BL4 at the ESRF, Grenoble. Substantial radiation damage was observed during data collection requiring that three crystals were used in total. Data collected from four crystal at Daresbury and the ESRF were merged together in SCALEPACK. Details of the data collection and processing statistics are given in Table 1.

Structure determination

The structure of the PP1-G_M[63-75] complex was solved by molecular replacement using as a model the protein atoms coordinates of the 2.5Å refined structure of the catalytic subunit of PP1γ1 determined by MAD methods (Egloff *et al.*, 1995). Rotation and translation functions searches were performed with AMORE (Navaza, 1992). Using data between 8 and 3 Å resolution, the peak in the rotation search was 6.7 standard deviations (SD) above the mean. The translation search was best performed using data between 8 and 3.5 Å, giving a maximal peak at 13.8 SD above the mean for the space group P41212. After the first rigid body refinement performed in AMORE, the R-factor was 0.494 and the correlation factor 0.30.

Crystallographic Refinement

The solution from molecular replacement was optimized by 20 cycles of rigid body refinement performed with X-PLOR version 3.1 (Brunger, 1992), using data between 8.0 Å and 3.0 Å resolution. After a round of conjugate gradient

positional refinement and simulated annealing molecular dynamics to 2000 K, followed by 25 cycles of grouped B-factor refinement (2 B-factor groups for each residue), the R factor (respectively free-R) was 0.295 (0.367). Fourier difference maps (Fo-Fc) and (3Fo-2Fc) revealed the presence of three strong peaks at (over three-times the sigma level of the map) at the catalytic site of PP1c. From the previously refined PP1c-structure, we identified two as manganese and iron ions. The third one, occupying the position of the tungstate ion in the PP1c-WO4 complex, was identified as sulphate. The initial difference Fourier maps also revealed strong electron density near the N-terminus of β14. The maps were improved by applying non-crystallographic symmetry 2-fold averaging using PHASES (Furey and Swaminathan, 1990). As shown in Fig. 1A, residues Val 66', Ser 67' and Phe 68' of the G_M[63-75] peptide were identified in the averaged map. These 3 residues, as well as the 2 metal and sulphate ions were built in each molecule, using the program TURBO-FRODO (Roussel and Cambillau, 1992). Refinement of this structure was performed by repeated rounds of manual rebuilding followed by conjugate gradient positional refinement and grouped B-factor refinement using X-PLOR. The final model contains protein residues Lys 6 to Ala 299 and peptide residues Arg 65' to Ala 69' in molecule 1, and protein residues Asn 8 to Lys 297 and peptide residues Gly 63' to Ala 69' in molecule 2. A few well defined water molecules were also observed in both initial (3Fo-2Fc) and (Fo-Fc) electron density maps. Eventually, 14 water molecules that were above 3 sigma in the (Fo-Fc) difference map, within hydrogen bond of the PP1-peptide complex or another solvent molecule and present in both molecules, were included in the model. The crystallographic and refinement data are summarized in Table 1. Representative electron density from the peptide before and after refinement is shown in Figure 10A and 10B, respectively. Solvent accessible surface areas were calculated using the method of Lee and Richards (1974).

Purification and assay of PP1.

PP1c was isolated from the rabbit skeletal muscle PP1-G_M complex as described previously (Johnson *et al*, 1996). Glycogen particles isolated from rat liver (Schelling *et al*, 1988) served as the source of PP1-G_L. The dephosphorylation of glycogen phosphorylase (10 μM) and the isolated MLC_{20} of smooth muscle myosin (1 μM) by PP1c was carried out as described previously (Cohen *et al.*, 1988; Alessi *et al.*, 1992).

Table 1. Crystallographic data and refinement statistics

Crystallographic data:	
Space group	$P4_12_12$
Unit cell parameters (Å)	a = b = 62.50; c = 361.30
Number of molecules per asymmetric unit	2
Temperature (K)	100
Total measured reflections	290671
Number of unique reflections	15509
Mean I/s(I)	7.5
Completeness (%)	87
Overall R-merge (%)	14.7
Refinement statistics:	
Number of reflections used for refinement	13078
Resolution range (Å)	8.0-3.0
R-work	0.223
R-free	0.308
Number of residues	<u>protein</u> <u>peptide</u>

Molecule 1	294 (Lys 6 to 6 (ARVSFA) (SEQ ID No 21) Ala 299) 6 (RRVSFA) SEQ ID No 3)
Molecule 2	290 (Asn 8 to Lys 297)
R.m.s.d. from ideal bond lengths (Å)	0.012
R.m.s.d. from ideal angles (°)	1.863
Number of water molecules	
Molecule 1	7
Molecule 2	7

Table 2. PP1-peptide polar interactions

	Peptide atom	Protein atom	Water molecule	Distance (Å)
Molecule 1	Arg 65′ O	-	7W	3.2
	Val 66′ N	Asp 242OD2 (**)		3.0
	Ser 67′ N	Leu 289 O		3.3
	Ser 67′ OG		7W	2.7
	Ser 67′ O	Cys 291 N (*)		3.2
	Ala 69′ N	Cys 291 O (*)		2.8
Molecule 2	Arg 64′ NH1	Glu 287 O		2.6
		(**)		
	Arg 65′ O		7W	2.8
	Val 66′ N	Asp 242 OD2 (**)		3.2
	Ser 67′ N	Leu 289 O (*)		3.1
	Ser 67′ OG		7W	2.6
	Ser 67′	Cys 291 N (*)		3.0

	Ala 69′ N	Cys 291 O (*)		3.3
Table 2. PP1-peptide hydrophobic interactions				
	Peptide residues	**Protein residues**		
	Val 66′	Ile 169 (*), Leu 243 (*), D242 (**), Leu 289 (*), Cys 291 (*)		
	Phe 68′	Phe 257 (*), Cys 291 (*), Phe 293 (*)		
	Ala 69′	Met290 (**)		

The star (*) indicates residues absolutely conserved in all protein phosphatase 1 sequences available so far, the double start (**) the residues mostly conserved (from sequence alignment from Barton *et al*, 1994).

RESULTS AND DISCUSSION

Structure Determination.

Crystallographic data to 3.0 Å were measured at the ESRF beam-line BL4 at Grenoble and at PX9.6, Daresbury (Table 1). The relatively high merging R-factors and low I/(I values of the crystallographic data results from the weak diffraction observed from the PP1-G_M[63-73] crystals. This is attributable to both the small crystal size (~25 μm by 25 μm by 5 μm) and long c-axis of the unit cell. In addition, the high x-ray photon dose required to obtain usable diffraction images resulted in x-ray radiation damage to the crystals, despite being maintained at a temperature of 100 K during the course of the experiment. The structure was solve by the molecular replacement method using as a search model the 2.5 Å refined coordinates of PP1c (Egloff *et al.*, 1995). Phases obtained from a single cycle of simulated annealing refinement

of the protein coordinates alone using X-PLOR Brunger, 1992), and improved by 2-fold non-crystallographic symmetry averaging and solvent flattening, were used to calculate an electron density map. This map revealed clear density corresponding to residues Val 66', Ser 67' and Phe 68' (where ' denotes residues of the peptide) of the G_M peptide and provided a starting point for further refinement of the PP1-G_M peptide complex (Fig. 10A). The final model of the complex was refined at 3.0 Å resolution with a crystallographic R-factor of 0.22 and R-free of 0.31 (Fig. 10B). The two molecules of PP1c within the asymmetric unit are similar with a root mean square deviation between main chain atoms of 0.6 Å. Residues 6 to 299 and 8 to 297 from molecules 1 and 2 respectively, are visible in the electron density map. Similar to the structures of native $PP_{\gamma 1}$ (Egloff *et al.*, 1995) and PP1α in complex with microcystin LR (Goldberg *et al.*, 1995), residues C-terminal to 299 are disordered.

Overall Structure of PP1

The conformation of PP1c in the PP1-G_M complex is virtually identical to that of native PP1c in complex with tungstate (Egloff *et al.*, 1995) with a root mean square deviation between equivalent main-chain atoms of 1.0 Å. PP1c is folded into a single elliptical domain consisting of a central β-sandwich of two mixed β-sheets surrounded on one side by 7α-helices and on the other by a sub-domain consisting of 3α-helices and a 3 stranded mixed α-sheet (Fig. 2A, B). The interface of the three β-sheets at the top of the β-sandwich creates a shallow catalytic site channel. Three loops connecting β-strands with α-helices within a β-α-β-α-β motif in sheet 1 (strand order β4-β3-β2-β13-β14) together with loops emanating from the opposite β-sheet (sheet 2; strand order, β1-β5-β6-β10-β12-β11) provide the catalytic site residues. The catalytic site of PP1 contains a binuclear metal site consisting of Mn^{2+} and Fe^{2+} (Egloff *et al.*, 1995) and, in the PP1-G_M complex, oxygen atoms of a sulphate ion of crystallisation coordinate both metal ions, similar to that seen in the PP1-tungstate (Egloff *et al.*, 1995) and PP2B-phosphate complexes (Griffith *et*

al, 1995).

PP1c-G_M[63-75] Peptide Interactions

Six residues of the G_M[63-75] peptide (Arg 64' to Ala 69') are clearly visible in the electron density map of the complex of molecule 2, the remaining residues are not visible and assumed to be disordered (Fig. 10B). Density is not visible for Arg 64' of the peptide bound to molecule 1, otherwise equivalent residues of the peptide are similar within the two complexes. The six residues (RRVSFA) (SEQ ID No 3) of the G_M[63-75] peptide in complex 2 adopt an extended conformation and bind to a hydrophobic channel on the protein surface with dimensions 25 Å by 10 Å that is formed at the interface of the two β-sheets of the β-sandwich opposite to the catalytic site channel and therefore remote from the catalytic site (Fig. 11A). The residues that form this channel occur on three regions of PP1c, namely (i) the N-terminus of 5 and β5/β6 loop of sheet 2; (ii) the three edge β-strands of sheet 2: β10, β12, β11 and (iii) β13, the β13/β14 loop and β14 of the edge of sheet 1 (Fig. 11A). The total solvent accessible surface area buried on formation of the complex is 980 Å2. Three residues of the peptide (Ser 67' to Ala 69') form a β-strand which is incorporated into β-sheet 1 of PP1c as a sixth β-strand parallel to the N-terminus of the edge β-strand, β14 (residues Leu 289 to Leu 296) (Fig. 11C). Main-chain atoms of Ser 67' and Ala 69' form H-bonds to the main-chain atoms of residues of β14. In addition, the main-chain nitrogen of Val 66' forms a H-bond with the side-chain of Asp 242. Other polar interactions include the guanidinium group of Arg 64' with the mainchain carbonyl of Glu 287 and a salt bridge to Asp 166. Both Asp 166 and Asp 242 are invariant in mammalian PP1 genes. A water molecule bridges the main-chain carbonyl of Arg 65' and side-chain hydroxyl of Ser 67' with the main-chain carbonyl of Thr 288 of PP1c (Fig. 11C). A notable feature of the peptide binding site is the presence of a negatively charged region created by seven acidic residues (with one Lys residue) surrounding the hydrophobic

channel at the N-terminus of the peptide in the vicinity of Arg 64' and Arg 65' that includes Asp 166 and Asp 242 (Fig. 11D). This would suggest a favourable electrostatic environment for the side chains of Arg 64' and Arg 65'.

The predominant interactions between the peptide and PP1c involve hydrophobic contacts between the side chains of Val 66' and Phe 68' and solvent exposed, invariant, hydrophobic residues of PP1c that form the hydrophobic channel (Fig. 11C, E). In particular, the binding site for the side chain of Val 66' is formed from the side chains of Ile 169, Leu 243, Leu 289 and Cys 291, whereas that for the side chain of Phe 68' is formed from the side chains of Phe 257, Cys 291 and Phe 293. Details of peptide-PP1c contacts are given in Table 2. The structure of the G_M[63-75] peptide binding site is likely to be conserved in other forms of PP1 from diverse species. Each hydrophobic residue of PP1c that interacts with the Val 66' and Phe 68' residues of the G_M[63-75] peptide are invariant and the acidic residues that surround the N-terminus of the peptide binding site are highly conserved amongst all isoforms of PP1 from species as diverse as yeast, *Drosophila*, mammals and higher plants (Barton *et al.*, 1994). However, since these residues are not conserved within the PP2A and PP2B sequences, these proteins will not recognise PP1-regulatory subunits.

Presence of an (R/K) (V/I) x F Motif in other PP1c Regulatory Proteins

Over a dozen regulatory subunits of PP1c are now known which appear to bind to PP1c in a mutually exclusive manner that suggests either an overlapping binding site or sites. Sequence comparisons of these subunits reveals little similarity except for the motif (R/K) (V/I) x F, that is not only present in G_M[63-75] but also in G_M, G_L, M_{110}, NIPP-1, p53BP2, and an RNA splicing factor (Fig. 12A). Moreover, a 38 residue peptide from the 110kDa M_{110} subunit that binds to PP1c contain this motif (Johnson *et al*, 1996), as do

fragments of NIPP-1 (Beullens *et al.*, 1992; Van Eynde *et al*, 1995), an RNA splicing factor (Hirano *et al.*, 1996) and p53BP2 (Helps *et al.*, 1995). A 32 residue peptide from p53BP2, which contains this motif, disrupted the interaction of the M_{110} subunit with PP1c, as shown by a decrease in the rate of dephosphorylation of the MLC_{20} subunit of smooth muscle myosin and by an increase in the rate of dephosphorylation of glycogen phosphorylase (Fig. 13A). This peptide also disrupted the interaction of the G_L subunit with PP1c, as shown by an increase in the rate of dephosphorylation of glycogen phosphorylase (Fig. 13B). Peptides comprising the motif (R/K) (V/I) x F are thus encompassed within the scope of the invention.

In further support of the notion of a common PP1c recognition motif present within PP1-binding proteins, previous studies had revealed that the sequence KIQF (SEQ ID No 22) (similar to the R/KVxF motif) at the N-terminus of inhibitor 1 and its homologue DARPP-32 (Fig. 12A) is necessary for mediating the inhibitory effects of these proteins. Loss of Ile 10 of the KIQF (SEQ ID No 22) motif of inhibitor 1 disrupts the inhibitory effects on PP1c by phospho-inhibitor-1 (Aitken and Cohen, 1984; Endo *et al.*, 1996) and the binding of either dephospho-inhibitor-1 or phospho-inhibitor-1 to PP1c (Endo *et al.* , 1996). A similar result was found on disrupting the equivalent residue (Ile 9) of DARPP-32 (Hemmings *et al.*, 1990; Desdouits *et al.*, 1995). These results were interpreted to indicate that inhibitor-1 and DARPP-32 bind to PP1 through two low affinity binding sites, one that encompasses the sequence KIQF (SEQ ID No 22) and another which includes the phosphorylated Thr residue (35 in I-1, 34 in DARPP-32) and which presumably binds at the catalytic site. Analysis of the PP1-G_M[63-75] complex structure suggests that an isoleucine residue could be readily accommodated within the peptide binding site in place of Val 66' such that the additional methyl group on Ile compared to Val would contribute to favourable van der Waals interactions between the peptide and Leu 243 and Cys 291 of PP1. More bulky hydrophobic residues

such as Leu, Met and Phe cannot be accommodated, however. It is interesting to note that as well as the (R/K) (V/I) x F motif shared by PP1-regulatory subunits, the four residues N-terminal to this motif contain an abundance of basic residues. These residues may provide further favourable interactions with the negative electrostatic surface potential at the N-terminus of the G_M(63-75] peptide binding site of PP1c (Fig. 11D).

Mutagenesis of the R/K) (V/I) x F motif

The structural studies presented here suggest a dominant role for Val 66' and Phe 68' in stabilising the interaction between G_M[63-75] and PP1c and this notion is further reinforced by the finding that other PP1-regulatory subunit sequences contain an (R/K)(V/I) x F motif yet share little overall sequence similarity. To test the hypothesis that Val 66' and Phe 68' are required for the interaction of G_M[63-75] with PP1c and also that the KVKF (SEQ ID No 5) sequence present within the M_{110}[M1-F38) peptide is important in mediating its interaction with PP1c, we synthesised variations of the G_M and M_{110} peptides where the R/KVxF motif was disrupted. The two variants of the G_M peptide were Val 66' and Phe 68' to Ala substitutions. In order to disrupt the (R/K)(V/I) x F present within the M_{110} peptide, a peptide corresponding to residues Met 1 to Lys 35 was synthesised which no longer contains the sequence VKF of the VxF motif, which is present at residues 36-38.

The results for the M_{110}[1-38] and M_{110}[1-35] peptides (Figs. 14, 15) are unequivocal. Whereas M_{110}[1-38] stimulates the myosin light chain phosphatase activity of PP1c with a half-maximal effect at 10 nM reaching maximal (3-fold) activation at a peptide concentration of 1 μM as reported previously (Johnson *et al*, 1996), the M_{110}[1-35] peptide was at least 104-fold less effective at activating PP1c (Fig. 14). Unlike M_{110}[1-38], the M_{110}[l-35] peptide was also unable to activate the phosphorylase phosphatase activity of liver PP1-G_L. This latter result suggests two conclusions. Firstly, that although M_{110}[1-38] is able

to bind to PP1c and disrupt the interactions between PP1c and the G_L-subunit, hence reversing the inhibitory effects of G_L on the ability of PP1c to dephosphorylate phosphorylase, loss of the VKF sequence in the M_{110}[1-38] peptide abolishes the ability of the peptide to disrupt this interaction. Secondly, the recognition site on PP1c for the VKF sequence of the M_{110}[1-38] peptide must overlap with the binding site for the G_L subunit, suggesting that the VKF sequence binds to the same site as the VSF sequence of G_L that is identical with that present in the G_M[63-75] peptide. Similar conclusions may be reached from the results obtained from disrupting the VxF motif within the G_M[63-75] peptide (Fig. 16B). Substitution of Phe 68' for Ala abolishes completely the ability of G_M[63-75] to disrupt the PP1-G_L complex, whereas replacement of Val 66' with Ala reduced the effectiveness of the disruption 100-fold.

Thus preferred peptides may comprise analogues of G_M with substitutions at Val 66' and Phe 68' to some other amino acid such as Ala, so that binding of the PP1c to G_M does not occur and the PP1c is not suitably directed or controlled. Alternatively, suitable peptides could comprise peptides suitable to compete for the binding site(s) of Val 66' and Phe 68' on PP1c. Such peptides can be added in sufficient quantities to compete for the Phe 68' and Val 66' binding site(s) on the PP1c, thereby disrupting the interaction of PP1c and natural G_M. Such peptides could comprise structural analogues of G_M with Phe 68' and Val 66' in the same positions as G_M. Alternatively, other amino acids capable of mimicking the binding of Phe 68' and Val 66' could be used in these locations.

Regulation of the PP1-G_M Complex by Phosphorylation of Ser 67'

Phosphorylation of Ser 67', corresponding to x of the VxF motif, by PKA promotes dissociation of both G_M and G_M[63-75] from PP1c. *In vivo*, this provides a mechanism of inhibiting PP1c during stimulation of skeletal muscle

by adrenalin (Dent *et al.*, 1990). The sequence of G_M surrounding Ser 67' (RRVSFA) (SEQ ID No 3) conforms to a consensus PKA recognition sequence. Interestingly, the conformation of the peptide is similar to that of residues 18 to 23 corresponding to the pseudo-substrate sequence of PKI bound to the catalytic site of PKA (Knighton *et al.*, 1990). Although the side chain of Ser 67' is exposed within the PP1c-peptide complex, overall the G_M peptide is buried, and it is unlikely that Ser 67' would be a substrate for PKA when the peptide is bound to PP1c. This would suggest that PKA phosphorylates Ser 67' when G_M is not associated with PP1c and that this phosphorylation prevents the re-association of PP1c with G_M. Since phosphorylation of Ser 67' promotes the dissociation of the PP1-G_M complex both *in vivo* and *in vitro*, it is most likely that PKA phosphorylates Ser 67' of G_M by competing with PP1c for the RRVSFA (SEQ ID No 3) sequence. This is consistent with a notion that the PP1-G_M complex exists in dynamic equilibrium with free PP1c and G_M subunits and that phosphorylation occurs on the regulatory subunit during transient dissociation from PP1c. In the PP1c-peptide complex, the side-chain of Ser 67' adopts the most favourable rotamer conformation. Analysis of the PP1c peptide complex structure suggests that incorporation of a phosphate group onto the side chain of Ser 67' with the same side-chain rotomer conformation would cause steric hindrance between the peptide and Met 290 of PP1 and also introduce a phosphate group into a region of negative charge at the PP1c surface (Fig. 11C, D). This may explain how phosphorylation of Ser 67' prevents peptide association with PP1c, although it should be noted that rotation of the side-chain of Ser 67' would relieve this steric clash.

A similar mechanism of control may also operate for other PP1-regulatory subunits. For example, NIPP-1 a nuclear inhibitor of PP1, inhibits PP1 with an inhibitory constant of 1 pM (Beullens *et al.*, 1992). Phosphorylation of NIPP-1 by PKA and/or casein kinase 2 *in vitro* abolishes this inhibition (Beullens *et al.*, 1993; Van Eynde *et al.*, 1994). Although the sites of

phosphorylation on NIPP-1 that mediate these effects are not yet fully characterised it is known that these sites occur within the central ~ 120 residues of NIPP-1 that incorporates the (R/K)(V/I) x F motif (Van Eynde *et al.*, 1995). Interestingly, a consensus phosphorylation site for PKA (RKNS) (SEQ ID No 23) occurs immediately N-terminal to this motif whereas one casein kinase 2 consensus phosphorylation site occurs between the Val and Phe of the motif and another occurs immediately C-terminal to the Phe residue (TFSEDDE) (SEQ ID No 24) (Van Eynde *et al.*, 1995) (Fig. 12A). It is possible that PKA, casein kinase II or other kinases with similar specificity, release PP1c from inhibition by NIPP-1 by phosphorylating NIPP-1 at sites that block its interaction with the (R/K)(V/I) x F motif recognition site on PP1c.

Model of the PP1c-Phospho-Inhibitor 1 Complex

Our model for the interaction of a (R/K)(V/I) x F motif with PP1c, together with previous kinetic data suggesting that the sequence KIQF (SEQ ID No 22) of inhibitor-1 (Aitken and Cohen, 1984; Endo *et al.*, 1996) and DARPP-32 (Hemmings *et al.*, 1990; Desdouits *et al*, 1995) interacts with PP1c, allowed us to construct a plausible model of a complex of PP1c with phospho-inhibitor 1. The major assumptions of this model were (1) the KIQF (SEQ ID No 22) sequence of inhibitor-1 binds to the same site as RVSF (SEQ ID No 25) of the G_M[63-75] sequence and (2) that the phosphothreonine residue 35 of phospho-inhibitor 1 binds at the phosphate binding site of the PP1c-catalytic site. Secondary structure predictions of inhibitor 1 (Rost and Sander, 1993; Rost, 1996) suggested that residues 9 to 14 and 23 to 31 adopt β-strand and α-helical conformations, respectively. The prediction of the sequence KIQF (SEQ ID No 22) as a β-strand is consistent with our assumption that this region of inhibitor-1 adopts the same conformation as RVSF (SEQ ID No 25) of the G_M peptide when bound to the VxF recognition site of PP1c. We have positioned the residues RRPpTP (SEQ ID No 26) encompassing the pThr 35

site within the catalytic site channel in an extended conformation, with the phosphate group of the pThr 35 occupying the phosphate binding site of the catalytic site and the Oγ-atom of Thr 35 equivalent to the solvent exposed oxygen of a dianion that forms a H-bond to the side-chain of the putative general acid His 125 (Egloff *et al.*, 1995; Griffith *et al.*, 1995). The four consecutive Arg residues N-terminal to pThr 35 interact with Asp and Glu residues within an acidic groove of PP1c formed from the $\beta7/\beta8$ loop on one side and the $\beta10/\beta11$ loop and $\beta11$ strand on the other, similar to that proposed by Goldberg *et al.*, (1995) for their model of DARPP-32 bound to PP1c. We propose that residues 20 to 30 of inhibitor-1 form an amphipathic helix which folds around the edge of the β-sandwich of PP1c. The N-terminus of this helix is disrupted by prolines at residues 19 and 23. Pro 19 and Pro 15 are probably responsible for introducing turns into the polypeptide chain that allows the β-strand encompassing the KIQF (SEQ ID No 22) sequence (residues 9 to 14) to connect with the α helix. The model of the phospho-inhibitor 1-PP1c complex is shown in Fig. 16.

Prediction of PP1 Recognition Motifs in Yeast PP1-Binding Proteins

The residues in mammalian PP1c that interact with the sequence RRVSFA (SEQ ID No 3) are conserved in *S. cerevisiae* PP1 suggesting that the proteins in *S. cerevisiae* known to interact with PP1 (reviewed by Stark, 1996) probably bind to a similar hydrophobic groove on the surface of the enzyme. Examination of their amino acid sequences revealed that a number of PP1-binding proteins in *S. cerevisiae* contained putative PP1-binding motifs that were similar to those present in mammalian PP1-binding proteins (Fig. 12A, B). The *S. cerevisiae* PP1-binding proteins not only contain a V/I x F motif, but also a basic residue equivalent to Arg 64' of G_MV the residue that contacts Asp 166, Leu 289 and the main-chain carbonyl of Glu 287 of PP1c. Several of the *S. cerevisiae* proteins also contain a further basic residue (His or Lys) at the position equivalent to Arg 65' of G_M. Another striking feature of the

putative PP1-binding sequences in *S. cerevisiae* is the presence of a basic amino acid between the Val/Ile and Phe residues, as is also found in two mammalian PP1-regulatory subunits, the M_{110} subunit and the p53BP2 (Fig. 12A).

The *S. cerevisiae* proteins GAC1 and PIG2 show some homology to residues 140-230 of mammalian G_MV and there is genetic and biochemical evidence that they may function to regulate glycogen metabolism in budding yeast (Francois *et al.*, 1992). GIP2 also shares sequence similarity with residues 140-230 of mammalian G_M, while YIL045W is an open reading frame in the *S. cerevisiae* genome whose predicted amino acid sequence shows 41% sequence identity to GIP2. YIL045W contains two putative PP1-binding motifs and site directed mutagenesis will be needed to establish which (if either) of these sequences binds to PP1c. REG1 and REG2 are PP1-binding proteins that play a role in cell growth and, in the case of REG1, glucose repression (Tu and Carlson, 1995; Tu *et al.*, 1996; Frederick and Tatchell, 1996). GIP1, which also contains two putative PP1-binding motifs, is expressed specifically during meiosis, affects the transcription of late meiotic genes and is essential for sporulation (Tu and Carlson, 1996). SCD5 is a PP1-interacting protein (Tu *et al.*, 1996) that was first isolated as a multicopy suppressor of the inviability of clathrin heavy chain-deficient yeast (Nelson *et al.*, 1996).

The findings herein demonstrate that the short peptide sequence, the (R/K)(V/I)XF motif, is critical for PP1c to interact with its regulatory subunits. PP1c (when complexed to its targeting subunits) plays key roles in the control of many cellular processed and it is reasonable to predict that over 100 pp1-binding proteins may exist in mammalian cells. Protein sequence data-base searching has revealed that the (R/K)(V/I)XF motifs are found in 10% of proteins. Thus if ~100 PP1-binding proteins occur in mammalian cells, only 1% of proteins with the (R/K)(V/I)XF motif will be PP1-binding proteins. The

reasons why only a few proteins with the (R/K)(V/I)XF motif bind to PP1 are numerous. For example, not every residue may be tolerated at position X or immediately N-terminal or C- terminal to this motif. This study has shown that phosphoserine is not tolerated at position X and it is therefore likely that Asp or Glu will not be tolerated either. The structure of the PP1-G_M[63-75] complex suggests that large hydrophobic residues will also be excluded from position X. Moreover, the Val (or Ile) and Phe residues in many (R/K)(V/I)XF motifs will be buried in the hydrophobic core of the protein and hence be unable to interact with PP1, since this motif is predicted to form an amphipathic β-strand conformation. Thirdly, many of the (R/K)(V/I)XF motifs will be in extracellular proteins or extracelluar domains of transmembrane proteins and hence be unable to bind to PP1. Particular feature so the tertiary structure of PP1-binding proteins may allow exposure of this motif on the surface to allow interaction with PP1. Finally, there is evidence that a second PP1-binding site exists on the G_M and M_{110} subunits (Johnson *et al.*, 1996) and the high affinity interaction of PP1c with protein inhibitor-1 is generated by the binding of PP1c to two low affinity sites (Desdouits *et al.*, 1995), one of which is the KIQF sequence belonging to the (R/K)(V/I)XF motif.

The question of how regulatory subunits modulate the substrate specificity of PP1c requires the co-crystallisation of PP1c with a diverse array of regulatory subunits and substrates and is beyond the scope of this paper. However, two models to account for this property of regulatory subunits are that these subunits either alter the conformation of PP1c or simply target PP1 to its substrates. Both mechanisms may operate *in vivo* depending on the regulatory subunits and substrates. For example, evidence for the former model has recently been reported for the enhancement of myosin dephosphorylation by a complex of PP1c and the M_{110} subunit (Johnson *et al.*, 1996, 1997), whereas the enhancement of the dephosphorylation of glycogen phosphorylase and glycogen synthase by the PP1-G_M complex is more consistent with the second

model (Hubbard and Cohen, 1989).

The identification of the (R/K)(V/I)XF motif also suggests a new approach for determining the physiological roles of PP1-targeting subunits whose functions are unknown. Thus mutation of the (R/K)(I/V)XF motif should disrupt the interaction of many targeting subunits with PP1c without affecting their binding to the target locus. Expression of these mutated proteins under an inducible promoter should lead to displacement of the normal targeting subunit (complexed to PP1c) from its target locus, without disrupting the functions of any other PP1c-targeting subunit complex. Finally, the structural information described here will also facilitate the rational design of drugs that act by disrupting PP1-targeting subunit interactions.

Example 3: Identification of the regions on the M_{110} subunit of protein phosphatase 1M that interact with the M_{21} subunit and with myosin

Abbreviations:- $PP1_M$, myofibril-associated form of protein phosphatase 1; PP1c, catalytic subunit of protein phosphatase-1; M_{110} and M_{21}, 110 kDa and 21 kDa regulatory subunits of $PP1_M$; MBP, maltose-binding protein; GST, glutathione-S-transferase.

SUMMARY

We have previously isolated a form of protein phosphatase-1 ($PP1_M$) from avian smooth muscle myofibrils which is composed of the catalytic subunit of PP1 (PP1c) bound to an M-complex consisting of 110 kDa (M_{110}) and 21 kDa (M_{21}) subunits. The interaction of PP1c with an N-terminal region of the M_{110} subunit enhances the dephosphorylation of myosin and suppresses the dephosphorylation of other substrates [Alessi, D.R., MacDougall, L.K., Sola, M.M., Ikebe, M. and Cohen, P. (1992) *Eur. J. Biochem* **210**, 1023-1035;

Chen, Y.H., Chen, M.X., Alessi, D.R., Campbell, D.G., Shanahan, C., Cohen, P. and Cohen, P.T.W. (1994) *FEBS Lett* **356**, 51-56; Johnson, D.F., Moorhead, G., Caudwell, F.B., Cohen, P., Chen, Y.H., Chen, M.X. and Cohen, P.T.W. (1996) *Eur. J. Biochem.* **239**, 317-325]. In this Example we establish that $PP1_M$ accounts for nearly all the myosin phosphatase activity in myofibrils, that the M_{110} and M_{21} subunits are present at similar concentrations in the myofibrillar fraction and that these subunits are entirely bound to PP1. We demonstrate that the M_{21} subunit does not interact with PP1c, but with the C-terminal 72 residues of the M_{110} subunit, a region which is 43% identical to residues 87-161 of the M_{21} subunit. A fragment of the M_{21} subunit, M_{21}-(M1-L146), lacking the C-terminal leucine zipper, also bound to the M_{110} subunit, but two other fragments M_{21}-(M1-E110) and M_{21}-(E110-K186) did not. The M_{110} and M_{21} subunits were both found to be myosin-binding proteins. The C-terminal 291 residues of the M_{110} subunit, but not the C-terminal 72 residues, bound to myosin, but the N-terminal fragments M_{110}-(M1-E309) and M_{110}-(M1-S477) did not. Thus the region of the M_{110} subunit which stimulates the dephosphorylation of myosin by PP1c is distinct from the region which targets $PP1_M$ to myosin. Remarkably, each myosin dimer was capable of binding about 20 moles of M_{21} subunit and many of the M_{21}-binding sites were located in the myosin "rod domain". The potential significance of this observation is discussed.

Introduction

Protein phosphatase-1 (PP1), one of the major serine/threonine-specific protein phosphatases in eukaryotic cells, is regulated by targetting subunits that direct it to particular subcellular loci, modify its substrate specificity and confer the ability to be regulated by extracellular signals (reviewed in [1, 2]). A significant proportion of the PP1 in vertebrate muscle extracts is associated with myofibrils and has enhanced activity towards the P-light chain of myosin and

reduced activity towards other substrates, such as glycogen phosphorylase [3, 4]. When isolated from avian (chicken gizzard) [4, 5] or mammalian (pig bladder) [6] smooth muscle, this form of PP1 ($PP1_M$) was found to be composed of three subunits, namely the catalytic subunit of PP1 (PP1c) and two other proteins with molecular masses of 110 kDa and 21 kDa, termed the M_{110} and M_{21} subunits, respectively [4, 5]. The M_{110} subunit is complexed to both PP1c and the M_{21} subunit [4], and is the component which modulates the substrate specificity of PP1c because selective removal of the M_{21} subunit from $PP1_M$ does not affect the rate at which either myosin or glycogen phosphorylase are dephosphorylated [7].

The M_{110} subunit has been cloned from rat aorta [5], chicken gizzard [8] and rat kidney [9] cDNA libraries. The N-terminus of the M_{110} subunit contains seven ankyrin repeats (residues 39-296 of the rat aorta protein), while alternative splicing in rat uterus [5] gives rise to two different C-termini (Fig 17A), termed Rat1 and Rat2. The C-terminus of Rat1 is virtually identical to the C-terminus of the M_{110} subunit from chicken gizzard (Fig 17A). The sequence of the M_{21} subunit from chicken gizzard is structurally related to the C-terminal region of the M_{110} subunit, the most striking similarities occurring from residues 76-141 of the M_{21} subunit and residues 921-984 of the chicken gizzard M_{110} subunit (54% identity, Fig 17B). However, the C-terminal 53 residues of the M_{21} subunit from chicken gizzard are strikingly similar (83% identity) to the C-terminal 53 residues of the rat aorta sequence, both terminating in a leucine zipper (Fig 17B, [5]).

Residues 1-309 of the M_{110} subunit from rat aorta, M_{110}-(M1-E309), mimic the intact M_{110} subunit in stimulating the dephosphorylation of myosin and in suppressing the dephosphorylation of glycogen phosphorylase by PP1c, but a slightly shorter construct M_{110}-(D39-E309) (which still contains the seven ankyrin repeats) is unable to modulate the specificity of PP1c [7]. This

observation led to the finding that the N-terminal 38 residues, M_{110}-(M1-F38), bind to PP1c and enhance the dephosphorylation of myosin. However, M_{110}-(M1-F38) does not suppress the dephosphorylation of glycogen phosphorylase, suggesting that the ankyrin repeats either contain a second PP1c-binding site or prevent glycogen phosphorylase from binding to the active site of PP1c, perhaps by steric hindrance [7].

A 13 residue peptide G_M-(G63-N75) from the subunit (G_M) which targets PP1c to glycogen and the sarcoplasmic reticulum in striated muscle, has been co-crystallised with PP1c and the structure of the complex solved to 3Å resolution [2]. These studies showed that a hexapeptide sequence in G_M-(G63-N75) (Arg-Arg-Val-Ser-Phe-Ala) (SEQ ID No 3) binds to a small hydrophobic groove on the surface of PP1c forming a β-sheet which runs parallel to another β-sheet in PP1c. Moreover, inspection of other mammalian PP1c-binding proteins reveals that almost all contain an Arg/Lys-Val/Ile-Xaa-Phe motif that is likely to be critical for interaction with PP1c [2]. For example, a Lys-Val-Lys-Phe (SEQ ID No 5) motif is present between residues 35 and 38 of the M_{110} subunit and the deletion of residues 36-38 from M_{110}-(M1-F38) prevents this peptide from stimulating the dephosphorylation of myosin, and from disrupting the interaction of PP1c with other targetting subunits [2].

The finding that a region near the N-terminus of the M_{110} subunit binds to PP1c and modulates its specificity raised the question of which region on the M_{110} subunit interacted with the M_{21} subunit, and how the $PP1_M$ complex is targeted to the myofibrils. In this Example we identify regions near the C-terminus of the M_{110} subunit that interact with the M_{21} subunit and with myosin, and demonstrate that the M_{21} subunit is also a myosin-binding protein. These findings indicate that the domain of the M_{110} subunit which enhances the dephosphorylation of the myosin P-light chain is distinct from the region which targets PP1c to the contractile apparatus.

MATERIALS AND METHODS

Materials

$PP1_M$ [4] and the dephosphorylated form of myosin [10] were isolated from chicken gizzard, and the rod-domain and light meromyosin were obtained by subdigestion of chicken gizzard myosin with papain and chymotrypsin, respectively [11]. $PP1_G$ was purified from rabbit skeletal muscle by Dr G. Moorhead in this laboratory [12] and PP1c dissociated from the glycogen-binding subunit by incubation for 2 h in 2 M LiBr and then purified by gel-filtration on a 30 x 1 cm column of Superose 12 (Pharmacia, Milton Keynes, UK) in the presence of LiBr (0.5 M). All other chemicals were from BDH Chemicals (Poole, UK) or Sigma (Poole, UK).

Construction of vectors for the expression of fragments of the M_{110} subunit from rat aorta (rat2 sequence in Fig 17A) as glutathione-S-transferase (GST) fusion proteins in E. coli.

A construct pGEX-M_{110}-(M1-E309) for the expression of GST-M_{110}-(M1-E309) from rat aorta was produced as described previously [7]. A construct for the expression of GST-M_{110}-(M1-S477) was prepared by subcloning a *Xho*I-*Hind*III fragment (encoding L24-S477) of pKS-M_{110}-(M1-S477) described in [5] into the same sites of pGEX-M_{110}-(M1-E309). The resulting construct expressed a GST-M_{110}-(M1-S477) fusion protein with the additional amino acids SAANSISSLIHRD* (SEQ ID No 27) after S477. An expression construct for GST-M_{110}-(M377-K976) was produced by deleting a *Nco*I-*Nco*I fragment of the construct pGEX-M_{110}-(L24-K976) [7].

Construction of vectors for the expression of C-terminal fragments of the M_{110} subunit from chicken gizzard (Ch1 sequence in Fig 17A, [5]) as maltose binding

protein (MBP) fusion proteins in E. coli.

A pT7.7 vector for the expression of the C-terminal 291 residues of the M_{110} subunit from chicken gizzard, pT7-M_{110}-(R714-I1004) was described previously [7]. A construct for the expression of MBP-M_{110}-(R714-I1004) was produced by cloning an *Nde*I-*Bam*HI fragment of pT7-M_{110}-(R714-I1004) into the pMAL-HA vector (New England Biolabs). Removal of a *Hin*dIII-*Hin*dIII restriction fragment from pMBP-M_{110}-(R714-I1004) allowed expression of MBP-M_{110}-(R714-L934) with the sequence GTGRRFTTS (SEQ ID No 28) added to its C-terminus. Removal of a *Nde*I-*Hin*dIII restriction fragment from pMBP-M_{110}-(R714-I1004), followed by filling in the overhanging ends and religating them, allowed expression of MBP-M_{110}-(K933-I1004).

Construction of vectors for the expression in E. coli. of the M_{21} subunit from chicken gizzard [5], with and without the C-terminal leucine zipper domain.

A pT7.7 vector for the expression of the entire coding region (M1-K186) of the M_{21} subunit was described previously [7]. The leucine zipper motif of the M_{21} subunit was deleted by removing a *Sac*I-*Bam*HI restriction fragment from pT7.7 M_{21}, filling in the overhanging ends and religating them. The construct expressed M_{21}-(M1-R144) with an extra I and L after residue 144. The M_{21}-(M1-R144) protein was insoluble when expressed and was purified as described for the expressed M_{21} subunit [7].

Construction of vectors for the expression of the M_{21} subunit from chicken gizzard [5] and fragments of the M_{21} subunit as glutathione-S-transferase (GST) fusion proteins in E. coli.

A construct expressing GST-M_{21} was produced by inserting a *Nde*I-*Hin*dIII fragment of pT7.7 M_{21} encoding M1-K186 into the same sites of the pGEX

vector modified to include an *Nde*I site. A construct expressing GST-M_{21}-(M1-E110) plus an additional Ala residue at the C-terminus was constructed by deleting a *Xho*I-*Hin*dIII fragment of pGEX-M_{21}, filling in the overhanging ends and religating them. In order to express GST-M_{21}-(E110-K186), a *NdeI-Xho*I restriction fragment of pGEX-M_{21} was deleted and the overhanging ends filled in and religated.

Expression of proteins in E. coli.

This was carried out essentially as described in [7], except that, after freezing the cells at -80°C and thawing, the lysates were not treated with DNAase but sonicated for 4 min on ice (ensuring that the temperature remained below 4°C) until the suspension was no longer viscous. The soluble GST-fusion proteins and MBP-fusion proteins were purified from the supernatant by affinity chromatography on glutathione-Sepharose (Sigma) and amylose resin (New England Biolabs), respectively, according to the instructions of the manufacturers. After expression in *E. coli* M_{110}-(R714-I1004) was the major soluble protein and all experiments with this fragment were performed using the bacterial extracts.

The chicken gizzard M_{21} subunit was isolated from *E. coli* extracts as described [7]. M_{21} subunit lacking the leucine zipper domain, M_{21}-(M1-L146), like the M_{21} subunit itself, was obtained in inclusion bodies and therefore recovered in the pellet obtained after centrifugation of the bacterial lysates for 30 min at 28 000 x g. The inclusion bodies were washed three times in 50 mM Tris/HCl pH 7.5, 0.1M NaCl, 10 mM EDTA, 0.1% (by vol) 2-mercaptoethanol, 1 mM benzamidine, 0.2 mM phenylmethylsulphonyl fluoride and 0.5% (by mass) Triton X-100, then resuspended in 50 mM Tris/HCl pH 7.5, 1 mM EDTA, 1 mM EGTA, 0.03% (by mass) Brij-35, 0.1% (by vol) 2-mercaptoethanol. An aliquot (containing 3 mg protein) was made 0.5% (by vol) in trifluoroacetic

acid, sonicated, centrifuged for 2 min at 13,000 x g and the supernatant (containing the solubilised M_{21} subunit) loaded on to a Vydac C18 column (Separations Group, Hesperia, CA, USA) equilibrated in 0.1% (by vol) trifluoroacetic acid. The column was developed with a linear acetonitrile gradient at a flow rate of 1.0 ml / min with an increase in acetonitrile concentration of 1% per min. Homogeneous M_{21} subunit, which eluted at 42% acetonitrile, and M_{21}-(M1-L146) which eluted at 40% acetonitrile were dried in a vacuum concentrator redissolved in water, redried and then dissolved in 50 mM Tris/HCl pH 7.5, 0.1 mM EGTA, 0.03% (by mass) Brij-35, 0.1% (by vol) 2-mercaptoethanol.

Removal of GST and MBP tags from fusion proteins.

GST-M_{110}-(1-477) was cleaved with thrombin and the proteinase removed using benzamidine agarose [7]. GST-M_{21}-(E110-K186) (1mg / ml) was cleaved by incubation for 1 h at 30°C with 10 μg/ml thrombin, while GST-M_{21}-(M1-E110) (1mg / ml) was cleaved by incubation for 3 h at 30°C with 1 μg/ml thrombin, because it was more susceptible to degradation by thrombin. MBP-M_{110}(K933-I1004) (1 mg / ml) was cleaved by incubation for 8 h at 23°C with Factor Xa (10 μg/ml). Other conditions and removal of Factor Xa were carried out as described for thrombin [7].

Preparation of phosphorylated myosin P-light chain and phosphatase assays.

^{32}P-labelled myosin P-light chains containing 1.0 mol phosphate per mol subunit was prepared by phosphorylation with smooth muscle myosin light chain kinase [4]. The dephosphorylation of myosin P-light chain (1 μM) was carried out as in [4] and one unit of activity (U) was that amount which catalysed the release of 1 μmole of phosphate in one min. When assaying $PP1_M$ in immunoprecipitates from the myofibrillar extracts, the tubes were

shaken continuously and 3 nM okadaic acid was included to inhibit any PP2A present.

Immunoprecipitation of $PP1_M$ from myofibrillar extracts.

Antibodies raised against the $PP1_M$ holoenzyme (1 μg), which recognise both the M_{110} and M_{21} subunits, but not PP1c, affinity purified antibodies specific for either the M_{110} subunit or M_{21} subunit (5 μg) [7], and control IgG (5 μg) were conjugated separately to 10 μl of pelleted protein G-Sepharose. After incubation for 30 min at 4°C, the Protein G-Sepharose-antibody conjugate was washed three times with 50 mM Tris/HCl pH 7.5, 0.1 mM EGTA, 0.03% (by mass) Brij-35, 0.3M NaCl, 0.1% (by vol) 2-mercaptoethanol before addition of a 100 μl of myofibrillar extract (prepared as in [4]) which had been diluted 10-fold in 50 mM Tris/HCl pH 7.5, 0.1 mM EGTA, 0.1% (by vol) 2-mercaptoethanol, 0.2 mM phenylmethylsulphonyl fluoride, 1 mM benzamidine, 10 μg/ml leupeptin containing 1 mg/ml bovine serum albumin. After incubation for 1 h at 4°C, with shaking, a 10 μl aliquot of the suspension was removed to measure the total activity. The remaining 90 μl was centrifuged for 1 min at 13,000 x g, the supernatant was removed, and the pellet washed twice in dilution buffer containing 0.2 M NaCl and 0.03% (by mass) Brij-35 (but no bovine serum albumin), once in dilution buffer and then resuspended in 90 μl of dilution buffer. Myosin P-light chain phosphatase activity was then measured in the supernatant and the resuspended pellet at a further 30-fold final dilution.

Myosin binding assays. Myosin (0.5 mg / ml, 1 μM in terms of myosin heavy chains) in 10 mM Hepes pH 7.5, 50 mM KCl, 5 mM MgCl2, 0.1% (by vol) 2-mercaptoethanol, was mixed with $PP1_M$, M_{21} subunit, or fragments of the M_{110} and M_{21} subunits, at the concentrations indicated in figure legends. After incubation for 15 min at 0°C, the solutions were centrifuged for 2 min at

13,000 x g, the supernatants removed, and the pellets washed twice in 10 mM Hepes pH 7.5, 50 mM KCl, 5 mM MgCl2, 0.1% (by vol) 2-mercaptoethanol before resuspension in 50 mM Tris-HCl pH 7.5, 0.1 mM EGTA, 0.03% (by mass) Brij 35, 0.6 M NaCl, 0.1% (by vol) 2-mercaptoethanol. Aliquots of the supernatant, the resuspended pellet and the suspension before centrifugation were either assayed for myosin P-light chain phosphatase activity or denatured in SDS and analysed by SDS/polyacrylamide gel electrophoresis.

Preparation of a complex between GST-M_{21} and M_{110}-(R714-I1004).

GST-M_{21} (10 μg) was mixed with 80 μl of bacterial extract expressing M_{110}-(R714-I1004). After incubation for 15 min at ambient temperature the solution was added to 20 μl (packed volume) of glutathione-Sepharose equilibrated in 50 mM Tris HCl pH 7.5, 0.1 mM EGTA, 0.03% (by mass) Brij 35, 0.1% (by vol) 2-mercaptoethanol, 0.2 mM phenylmethylsulphonyl fluoride, 1 mM benzamidine and 0.15 M NaCl. After incubation for 30 min at 4°C with shaking, the Sepharose was washed three times in the same buffer before eluting the complex with buffer containing 20 mM glutathione pH 8.0.

Other procedures.

Proteins were labelled with digoxigenin and Far Western analyses carried out as described [4], except that the digoxigenin-labelled probe was used at a concentration of 0.2 μg/ml instead of 2 μg/ml. SDS/polyacrylamide gel electrophoresis was carried out on 7.5-15% gels according to Laemmli [13] and on 16.5% gels according to Schagger and von Jagow [14]. Protein was estimated according to Bradford [15].

Results

$PP1_M$ accounts for nearly all the myosin phosphatase activity in extracts prepared from chicken gizzard myofibrils.

80-90% of the myosin phosphatase activity present in chicken gizzard homogenates is recovered in the myofibrils [4]. In the present study, we used antibodies that recognise the M_{110} and/or the M_{21} subunits of chicken gizzard $PP1_M$ [7] to immunoprecipitate the myosin P-light chain phosphatase activity from the myofibrillar extracts. About 90% of the activity was immunoprecipitated by antibodies raised against the $PP1_M$ holoenzyme (Fig 18A) which recognise both the M_{110} and M_{21} subunits in immunoblotting experiments, but not PP1c. Similarly, about 80% of the myosin P-light chain phosphatase activity in the myofibrillar extracts was immunoprecipitated by either the anti-M_{110} antibody or by the anti-M_{21} antibody (Fig 18A). Thus, most of the myosin P-light chain phosphatase activity in myofibrillar extracts is catalysed by PP1c present as a complex containing both the M_{110} and the M_{21} subunits.

Immunoblotting experiments demonstrated that the ratio M_{110}:M_{21} in myofibrillar extracts was identical to the ratio of these subunits in purified $PP1_M$ (Fig 18B), which is 1:1 [4]. These immunoblotting experiments also demonstrated that $PP1_M$ comprises 0.1% of the protein in the myofibrillar extract (see legend to Fig 18B), identical to the proportion estimated from the fold-purification needed to obtain pure $PP1_M$ from this fraction (see Table 1 in Ref 4). These experiments imply that $PP1_M$ accounts for virtually all the myosin phosphatase activity associated with myofibrils, and that neither the M_{110} nor the M_{21} subunit is present in a significant molar excess over PP1c in the myofibrils.

Identification of a region on the M_{110} subunit that binds to the M_{21} subunit.

$PP1_M$ and several fragments of the M_{110} subunit, were subjected to SDS/polyacrylamide gel electrophoresis (Fig 19A) and, after transfer to nitrocellulose, the blots were probed with digoxigenin-labelled M_{21} subunit (Fig 19B). These experiments showed that the M_{21} subunit recognised the full length M_{110} subunit (Fig 19B, track 1), M_{110}-(R714-I1004) (Fig 19B, tracks 2 and 3) and M_{110}-(K933-I1004) (Fig 19B, track 5), but not M_{110}-(R714-L934) (Fig 19B, track 4), M_{110}-(M1-E309) (Fig 19B, track 7) or M_{110}-(M1-S477) (Fig 19B, track 8). Thus, the M_{21} subunit binds to the C-terminal 72 residues of the M_{110} subunit. The specificity of this interaction was indicated by the observation that digoxigenin-labelled M_{21} subunit recognised only M_{110}-(R714-I1004) and no other protein in the *E. coli* extract (track 2 in Figs 19A and 19B), nor did it recognise the MBP or GST tags, PP1c (Figs 19A and 19B) or any of the molecular mass markers (data not shown).

Consistent with the results in Fig 19, digoxigenin-labelled MBP-M_{110}-(R714-I1004) (data not shown) and MBP-M_{110}-(K933-I1004) (Fig 20B), but not digoxigenin-labelled MBP-M_{110}-(R714-L934) (data not shown), recognised the full length M_{21} subunit and M_{21}(M1-L146) in Far Western blotting experiments.

The region of the M_{21} subunit that interacts with the M_{110} subunit.

Digoxigenin-labelled M_{21}-(M1-L146) recognised the same fragments of the M_{110} subunit as the full length M_{21} protein (Fig 19C), demonstrating that the C-terminal leucine zipper of the M_{21} subunit is not required for interaction with the M_{110} subunit. However, neither digoxigenin-labelled GST-M_{21}-(M1-E110) nor digoxigenin-labelled GST-M_{21}-(E110-K186) recognised M_{110}-(K933-I1004) in Far Western blotting experiments (data not shown). Consistent with these findings, digoxigenin-labelled M_{110}-(K933-I1004) recognised the full length M_{21}

protein and M_{21}-(M1-L146), but not M_{21}-(M1-E110) or M_{21}-(E110-K186) in Far Western blotting experiments (Figs 20A and B). However, digoxigenin-labelled M_{110}-(K933-I1004) did recognise a proteolytic fragment of the M_{21} subunit with an apparent molecular mass only slightly larger than M_{21}-(M1-E110) (Fig 20B, track 2 and compare tracks 2 and 4 in Fig 20A). These results are considered further under Discussion.

The isolated M_{21} subunit dimerizes and the region involved in dimerization is identical to that which interacts with the M_{110} subunit.

Although the M_{110} subunit binds to both PP1c and the M_{21} subunit [4], and removal of the M_{21} subunit does not alter the specificity of the $PP1_M$ complex [7], an interaction between the M_{21} subunit and PP1c had not been excluded. In order to examine this point, PP1c and the M_{21} subunit were mixed together and subjected to gel filtration on Superose 12. The M_{21} subunit eluted just before the 37 kDa PP1c protein, demonstrating that they do not form a high affinity complex and suggesting that the isolated M_{21} subunit dimerizes (data not shown). These results were supported by the finding that digoxigenin-labelled full length M_{21} subunit recognised the M_{21} subunit as well as the M_{110} subunit, but not PP1c, in Far Western blotting experiments (Fig 21, track 1). Similar results were obtained with M_{21}-(M1-L146) (Fig 21, track 2). Digoxigenin-labelled M_{21} subunit, like digoxigenin-labelled M_{110}-(K933-I1004), recognised a fragment of the M_{21} subunit that migrated slightly more slowly than M_{21}-(M1-E110), but did not recognise M_{21}-(M1-E110) or M_{21}-(E110-K186) (Tracks 2, 4 and 5 in Figs 20B and 20C).

Identification of a region on the M_{110} subunit that binds to myosin.

When $PP1_M$ (30 nM) was mixed with chicken gizzard myosin (1 μM) and centrifuged to pellet the myosin, 85% of the myosin P-light chain phosphatase

was recovered in the pellet (Figs 22 and 23A). In contrast, neither PP1c (Fig 22) nor bovine serum albumin (data not shown) bound to myosin under these conditions. After removal of the M_{21} subunit from $PP1_M$ [7], the M_{110}-PP1c complex ($PP1_M(\Delta M_{21})$) still pelleted with myosin in a similar manner to $PP1_M$ itself (Fig 22), indicating that the M_{110} subunit is a myosin-binding protein.

In order to identify the myosin-binding domain(s), several fragments of the M_{110} subunit were expressed and purified from *E. coli* extracts and their binding to myosin was studied. GST-M_{110}-(M1-S477), like GST-M_{110}-(M1-E309) [7], stimulated the PP1c-catalysed dephosphorylation of the myosin P-light chain and inhibited the dephosphorylation of glycogen phosphorylase in a similar manner to the full length M_{110} subunit (data not shown). However, neither GST-M_{110}-(M1-S477) nor GST-M_{110}-(M1-E309) bound to myosin (data not shown), even after removal of the GST-tag from GST-M_{110}-(M1-S477) (Fig 23A).

A fragment comprising GST-M_{110}-(M377-K976) from rat aorta migrated as multiple bands on SDS/polyacrylamide gels after purification on glutathione-Sepharose (Fig 23A), indicating cleavage at multiple sites within the M_{110} subunit. Only the largest fragment, with an apparent molecular mass corresponding to undegraded GST-M_{110}-(M377-K976) bound to myosin (Fig 23A), suggesting that the myosin binding site(s) was located towards the C-terminus of the M_{110} subunit. Consistent with this finding, M_{110}-(R714-I1004) from chicken gizzard also bound to myosin (Fig 23B). However, M_{110}-(K933-I1004), which bound to the M_{21} subunit (Fig 20B), did not bind to myosin in these experiments (Fig 23B).

The M_{21} subunit, and a complex between M_{21} and M_{110}-(R714-I1004) bind to myosin.

After purification on glutathione-Sepharose, GST-M_{21} migrated as four protein staining bands (track 1 in Fig 20A), the two species of highest apparent molecular mass being recognised by the anti-M_{21} antibody (Fig 23B). The apparent molecular mass of the slowest migrating band (47 kDa) corresponds to undegraded GST-M_{21} and this species bound to myosin (Fig 23B). The next most slowly migrating band had an apparent molecular mass of 38 kDa, slightly less than that of GST-M_{21}-(M1-E110) (data not shown) indicating that it corresponds to GST fused to about the first 100 residues of the M_{21} subunit; this fragment hardly bound to myosin (Fig 23B).

Bacterial extracts expressing M_{110}-(R714-I1004) were mixed with GST-M_{21} and the resulting complex was purified on glutathione-Sepharose. This complex bound quantitatively to myosin (Fig 23B). In contrast, the GST-M_{21} fragment of apparent molecular mass 38 kDa was not complexed to M_{110}-(R714-I1004) and did not bind to myosin (Fig 23B). The C-terminal fragment of the M_{21} subunit, M_{21}-(E110-K186) also did not bind to myosin under these conditions (data not shown).

Multiple binding sites for the M_{21} subunit on the myosin molecule.

The molar ratio myosin:$PP1_M$ in chicken gizzard is about 80:1 *in vivo* [4] and the myosin binding experiments described above were therefore carried out using a large (ten fold) molar excess of myosin over either the M_{21} or the M_{110} subunit. However, further experiments carried out with the M_{21} subunit in excess revealed that, remarkably, 20 or more moles of M_{21} subunit could be bound to each myosin dimer (Fig 24A). Many of the binding sites were located in the region of myosin involved in filament formation, because the M_{21}

subunit was pelleted with the myosin "rod" domain even when the molar ratio M_{21}: myosin dimer was 10:1 (Fig 24B). A shorter portion of the rod, termed light meromyosin, also bound the M_{21} subunit avidly. However, a fragment of the M_{21} subunit lacking the first 15 residues from the N-terminus, which was a contaminant in this preparation, did not bind to light meromyosin (Fig 24B), although it bound to the longer myosin rod (Fig 24B). The M_{21} subunit lacking the C-terminal leucine zipper, M_{21}-(M1-L146), bound to both myosin and the rod domain, but fewer moles of M_{21}-(M1-L146) could be bound and this C-terminally truncated species did not bind to light meromyosin under the conditions studied (Fig 24C).

Multiple forms of the M_{110} subunit

Comparison of two different clones encoding the M_{110} subunit from chicken gizzard revealed a 123 bp (41 amino acid) deletion/insertion after Asn-511 (Fig 17, [8]). Since the rat aorta sequence [5] showed considerable variation from the chicken sequences in this region, compared to the high degree of sequence similarity throughout most of the rest of the molecule (Fig 17), it seemed probable that forms of the rat M_{110} subunit also existed that varied in this middle section of the protein. PCR of the "variable region" of several rat aorta clones gave fragments of either 608 bp or 776 bp. Direct sequencing of these fragments showed an in frame insertion of 168bp (56 amino acids) after Ser-552 (Fig. 1); i.e. a slightly different position from the deletion reported for the chicken gizzard M_{110} subunit (Fig 17). Furthermore, a different 62 amino acid deletion/insertion in this section is apparent by comparison of the rat aorta sequences with that of the M_{110} protein from rat kidney (Fig. 1) [9]. While it is likely that most of these variations arise by alternative splicing of the mRNA, Southern blotting of rat genomic DNA revealed the presence of two closely related genes (data not shown).

Discussion

The contraction of smooth muscle is triggered by phosphorylation of the P-light chain of myosin catalysed by myosin light chain kinase. However, the identity of the myosin P-light chain phosphatase remained unclear for many years. In 1992 we reported that 80-90% of the myosin phosphatase activity in chicken gizzard homogenates was associated with myofibrils and purified a myosin phosphatase to homogeneity from this fraction [4]. This enzyme, termed $PP1_M$, was found to be composed of the β-isoform of PP1c (termed the δ-isoform in [16]) and an "M-complex" consisting of two other subunits [4] whose molecular masses were 21 kDa (M_{21}) [5] and 110 kDa (M_{110}) [5, 8], respectively. Further evidence that a form of PP1 was the major myosin phosphatase in smooth muscle was indicated by the finding that tautomycin (a much more potent inhibitor of PP1 than PP2A [17]) stimulated the contraction of permeabilised mammalian smooth muscle fibres at much lower concentrations than okadaic acid [18] (a much more potent inhibitor of PP2A than PP1 [19]).

Two further pieces of evidence presented in this Example establish that $PP1_M$ accounts for most, if not all, of the myosin phosphatase activity associated with chicken gizzard myofibrils, reinforcing the view that it is likely to be the major myosin P-light chain phosphatase *in vivo*. Firstly, nearly all the myosin P-light chain phosphatase activity was immunoprecipitated by antibodies that recognise either the M_{110} or the M_{21} subunit specifically (Fig 18A). Secondly, $PP1_M$ was found to represent 0.1% of the protein in the myofibrillar extracts whether its concentration was calculated from the increase in specific activity needed for purification to homogeneity [4] or from immunoblotting experiments with the anti-M_{110} and anti-M_{21} antibodies (Fig 18B). Had another enzyme been the major myosin phosphatase in the myofibrillar extracts the enrichment estimated by immunoblotting with anti-M_{110} and anti-M_{21} antibodies would have been

much higher.

The experiments presented in Fig 18 also demonstrate that the M_{110} and M_{21} subunits are not present in myofibrillar extracts in a significant molar excess over PP1c and that all the M_{110} subunits are complexed to M_{21} subunit and vice versa. The M_{21} subunit was found to bind to the C-terminal 72 residues of the chicken gizzard M_{110} subunit (Figs 19 and 25), a region whose amino acid sequence is 43% identical to residues 87-161 of the M_{21} subunit (Fig 17B). The C-terminal leucine zipper of the M_{21} subunit (residues 145-186) is not required for interaction with the M_{110} subunit, and the site on the M_{21} subunit which interacts with the M_{110} subunit lies within about the N-terminal 120 residues (Fig 20B). Interestingly, the same region is essential for the dimerisation of the M_{21} subunit (compare Figs 20B and 20C), suggesting that the region(s) involved in interaction is probably located between residues 60 and 120 of the M_{21} subunit and 906-965 of the M_{110} subunit from chicken gizzard; i.e. the regions with greatest amino acid identity between these two proteins (Fig 17). More digoxigenin-labelled M_{21} subunit bound to the M_{110} subunit than to the M_{21} subunit in Far Western blotting experiments (Fig 21), consistent with the observation that M_{110}/M_{21} heterodimers form *in vivo*, but not M_{21}/M_{21} homodimers. The finding that the C-terminus of the M_{110} subunit interacts with the M_{21} subunit explains why preparations of $PP1_M$ comprising PP1c complexed to N-terminal fragments of the M_{110} subunit do not contain the M_{21} subunit [8, 20].

$PP1_M$ binds to the dephosphorylated form of myosin and our data demonstrate that the M_{110} subunit (Fig 22) and the M_{21} subunit (Fig 23B and Fig 24) are both myosin-binding proteins. The C-terminal 600 residues of the M_{110} subunit from rat aorta, M_{110}-(M377-K976) (Fig 23A) and the C-terminal 291 residues of the M_{110} subunit from chicken gizzard, M_{110}-(R714-I1004), bound to myosin, but the C-terminal 72 residues of the M_{110} subunit, M_{110}-(K933-1004), did not

(Fig 23B), indicating that a myosin-binding domain is likely to be situated in the M_{110} subunit just N-terminal to the M_{21}-binding domain (Fig 25). In contrast, two N-terminal fragments of the M_{110} subunit M_{110}-(M1-S477) (Fig 23A) and M_{110}-(M1-E309) (data not shown) did not bind to myosin under the conditions studied. Since M_{110}-(M1-E309) [7] and M_{110}-(M1-S477) (data not shown) stimulate the dephosphorylation of myosin and inhibit the dephosphorylation of glycogen phosphorylase by PP1c, and in a similar manner to full length M_{110} subunit, these results show that the region of the M_{110} subunit which stimulates the dephosphorylation of the myosin P-light chain is distinct from that which binds the dephosphorylated form of myosin and thereby targets $PP1_M$ to the contractile apparatus.

Digestion of chicken gizzard $PP1_M$ with chymotrypsin cleaves the M_{110} subunit to a fragment with an apparent molecular mass of 58 kDa and a form of PP1, termed here $PP1_M$*, can then be isolated by gel-filtration which appears to comprise just the 58 kDa fragment and PP1c in a 1:1 molar ratio [8]. The 58 kDa fragment, like the M_{110} subunit, has a blocked N-terminus and seven tryptic peptides isolated were located between residues 286 and 467, suggesting that the 58 kDa fragment corresponds to the N-terminal portion of the M_{110} subunit [8]. $PP1_M$* was reported to bind to myosin, albeit less effectively than $PP1_M$ [8], suggesting the presence of a myosin-binding domain within the 58 kDa fragment. This result is in apparent conflict with the present study, because the fragment M_{110}-(M1-S477), which also migrates on SDS/polyacrylamide gels with an apparent molecular mass of 58 kDa, did not bind to dephosphorylated myosin under conditions where 80-90% of the $PP1_M$ and M_{110}-(R714-I1004) was pelleted with myosin (Fig 23A). One possible explanation for this discrepancy is that $PP1_M$* also contains small myosin-binding fragments from the C-terminus of the M_{110} subunit which still interact with the N-terminal 58 kDa fragment, but are too small to be detected by SDS/polyacrylamide gel electrophoresis. In a separate study heavy meromyosin

(50 μg) was found to bind partially to 2 mg of M_{110}-(1-633) coupled to Affigel 15, at very low ionic strength but not at 150-200 mM NaCl [21]. The significance of this observation is unclear because of the extremely high concentration of the M_{110}-(1-633) used in these experiments. The average intracellular concentration of $PP1_M$ in chicken gizzard is about 1 μM, 100-fold lower than the concentration of myosin. In the present study, we analysed the binding of the M_{110} subunit and its subfragments (30-100 nM) to myosin (1 μM) using low concentrations of these proteins to try and ensure that only high affinity binding sites were identified.

The isolated M_{21} subunit also bound to myosin and up to 20 moles of M_{21} subunit could be bound to each myosin dimer (Fig 24). These observations indicate that each myosin molecule contains multiple binding sites for the M_{21} subunit, many of which are located within the "rod domain" (Figs 24B and 24C). *In vivo*, the molar ratio $PP1_M$: myosin is about 1:80 and yet, during muscle relaxation, all the myosin P-light chains can be dephosphorylated by $PP1_M$ within seconds. This implies that $PP1_M$ must be highly mobile within the myofibrils and move extremely rapidly from one myosin molecule to another. The "off rates" for binding of $PP1_M$ to myosin must therefore be very fast as well as the "on rates". It is tempting to speculate that the presence of multiple binding sites on myosin for the M_{21} subunit (and perhaps for the M_{110} subunit as well) allows $PP1_M$ to "slide" rapidly from one myosin molecule to another.

<u>Example 4: Design of small molecules to modulate the properties of PP1</u>

Table A is a print-out of the atomic coordinates of the protein phosphatase-1 peptide coordinates as deduced in Example 2. The format is Protein Data Bank. The structure of the protein phosphatase-1 catalytic subunit (PP1c) in complex with a 13-residue peptide (G_M peptide) corresponding to a site of interaction between PP1c and the glycogen targeting subunit provides a frame-

work for the rational design of small molecules to modulate the functions and properties of PP1 *in vivo*. Knowledge of the structural nature of the interactions between the G_M peptide and PP1c allows the design of inhibitors that mimic these interactions. These inhibitors may be designed for increased potency, cell permeability and with improved pharmokinetic properties.

Computer graphics systems may be used to design such inhibitors in conjunction with computer graphics modelling software such as SYBIL available from: Tripos Inc, 16995 S Hanley Road, St Louis, Missouri 63144-2913, USA and LUDI available from: Molecular Simulations Inc, 9685 Scranton Road, San Diego, CA 92121-3752, USA, and in conjunction with the atomic coordinates shown in Table A.

Example 5: Effect of peptide derived from p53BP2 binding site to PP1 *in vivo*

The function of p53BP2 is ascertained by examining the *in vivo* effect of peptides based on the sequence of the p53BP2 binding site to PP1. This may be done by reference to the consensus peptide sequence described in the previous Examples and by reference to the crystal structure in Example 2. The peptide is introduced into cultured cells using penetratin available from Appligene. Other importins may also be used. Alternatively cDNA specifying p53BP2 proteins mutant in the p53BP2 binding site to PP1 are transfected in cultured cells. The effect of these agents on the cell cycle and apoptosis are assessed by a number of methods, for example WAF1 ELISA and Nuclear Matrix Protein ELISA assays (Amersham).

The effect of the p53BP2 peptide is to modulate the interaction between PP1 and p53BP2 *in vivo* and affect cell regulation and apoptosis. The p53BP2 peptide may also be micro-injected into the cell.

Table A

ATOM	1	N	LYS	6	-10.263	46.372	91.126	1.00	53.07	0
ATOM	3	CA	LYS	6	-9.182	46.177	90.159	1.00	53.07	0
ATOM	4	CB	LYS	6	-9.220	47.277	89.092	1.00	45.20	0
ATOM	5	CG	LYS	6	-10.284	47.095	88.015	1.00	45.20	0
ATOM	6	CD	LYS	6	-9.809	46.200	86.868	1.00	45.20	0
ATOM	7	CE	LYS	6	-8.832	46.919	85.927	1.00	45.20	0
ATOM	8	NZ	LYS	6	-7.498	47.216	86.540	1.00	45.20	0
ATOM	12	C	LYS	6	-7.814	46.179	90.835	1.00	53.07	0
ATOM	13	O	LYS	6	-6.854	45.624	90.303	1.00	45.20	0
ATOM	14	N	LEU	7	-7.746	46.816	92.005	1.00	42.33	0
ATOM	16	CA	LEU	7	-6.527	46.941	92.800	1.00	43.14	0
ATOM	17	CB	LEU	7	-6.840	47.599	94.141	1.00	24.45	0
ATOM	18	CG	LEU	7	-5.670	47.782	95.106	1.00	18.34	0
ATOM	19	CD1	LEU	7	-4.775	48.881	94.589	1.00	25.09	0
ATOM	20	CD2	LEU	7	-6.186	48.121	96.496	1.00	22.21	0
ATOM	21	C	LEU	7	-5.892	45.594	93.063	1.00	42.81	0
ATOM	22	O	LEU	7	-6.497	44.723	93.675	1.00	23.55	0
ATOM	23	N	ASN	8	-4.656	45.424	92.627	1.00	17.03	0
ATOM	25	CA	ASN	8	-4.000	44.156	92.846	1.00	11.65	0
ATOM	26	CB	ASN	8	-3.204	43.744	91.610	1.00	18.54	0
ATOM	27	CG	ASN	8	-3.486	42.312	91.193	1.00	15.30	0
ATOM	28	OD1	ASN	8	-4.643	41.903	91.068	1.00	14.53	0
ATOM	29	ND2	ASN	8	-2.429	41.538	90.993	1.00	7.61	0
ATOM	32	C	ASN	8	-3.110	44.207	94.079	1.00	11.35	0
ATOM	33	O	ASN	8	-1.906	44.515	93.985	1.00	12.23	0
ATOM	34	N	ILE	9	-3.716	43.900	95.232	1.00	12.56	0
ATOM	36	CA	ILE	9	-3.018	43.894	96.523	1.00	14.41	0
ATOM	37	CB	ILE	9	-3.955	43.439	97.690	1.00	2.00	0
ATOM	38	CG2	ILE	9	-3.155	42.828	98.812	1.00	2.00	0
ATOM	39	CG1	ILE	9	-4.742	44.634	98.244	1.00	2.00	0
ATOM	40	CD1	ILE	9	-3.865	45.837	98.581	1.00	2.00	0
ATOM	41	C	ILE	9	-1.796	42.996	96.501	1.00	10.07	0
ATOM	42	O	ILE	9	-0.759	43.351	97.045	1.00	2.00	0
ATOM	43	N	ASP	10	-1.916	41.845	95.849	1.00	2.00	0
ATOM	45	CA	ASP	10	-0.822	40.887	95.782	1.00	2.00	0
ATOM	46	CB	ASP	10	-1.336	39.562	95.208	1.00	45.77	0
ATOM	47	CG	ASP	10	-2.234	38.801	96.191	1.00	46.34	0
ATOM	48	OD1	ASP	10	-3.054	39.444	96.879	1.00	50.94	0
ATOM	49	OD2	ASP	10	-2.123	37.558	96.281	1.00	55.84	0
ATOM	50	C	ASP	10	0.426	41.369	95.036	1.00	2.00	0
ATOM	51	O	ASP	10	1.540	41.181	95.516	1.00	43.44	0
ATOM	52	N	SER	11	0.245	41.993	93.874	1.00	2.00	0
ATOM	54	CA	SER	11	1.387	42.494	93.112	1.00	2.00	0
ATOM	55	CB	SER	11	0.987	42.834	91.678	1.00	24.54	0
ATOM	56	OG	SER	11	-0.025	43.819	91.653	1.00	26.40	0
ATOM	58	C	SER	11	1.964	43.727	93.804	1.00	2.00	0
ATOM	59	O	SER	11	3.168	44.010	93.702	1.00	23.86	0
ATOM	60	N	ILE	12	1.099	44.467	94.493	1.00	19.26	0
ATOM	62	CA	ILE	12	1.536	45.641	95.226	1.00	19.26	0
ATOM	63	CB	ILE	12	0.345	46.351	95.878	1.00	2.00	0
ATOM	64	CG2	ILE	12	0.831	47.364	96.909	1.00	2.00	0
ATOM	65	CG1	ILE	12	-0.499	46.986	94.775	1.00	2.00	0
ATOM	66	CD1	ILE	12	-1.722	47.687	95.245	1.00	2.00	0
ATOM	67	C	ILE	12	2.501	45.112	96.275	1.00	19.26	0
ATOM	68	O	ILE	12	3.684	45.445	96.264	1.00	2.00	0
ATOM	69	N	ILE	13	1.987	44.246	97.141	1.00	2.00	0
ATOM	71	CA	ILE	13	2.764	43.605	98.199	1.00	2.00	0
ATOM	72	CB	ILE	13	1.899	42.504	98.897	1.00	2.00	0
ATOM	73	CG2	ILE	13	2.747	41.645	99.810	1.00	2.00	0
ATOM	74	CG1	ILE	13	0.764	43.154	99.691	1.00	2.00	0
ATOM	75	CD1	ILE	13	-0.213	42.167	100.331	1.00	2.00	0
ATOM	76	C	ILE	13	4.039	42.960	97.602	1.00	2.00	0
ATOM	77	O	ILE	13	5.142	43.099	98.158	1.00	2.00	0
ATOM	78	N	GLN	14	3.864	42.278	96.462	1.00	2.00	0
ATOM	80	CA	GLN	14	4.937	41.582	95.740	1.00	2.00	0
ATOM	81	CB	GLN	14	4.415	41.065	94.391	1.00	21.13	0
ATOM	82	CG	GLN	14	5.467	40.470	93.454	1.00	32.43	0
ATOM	83	CD	GLN	14	5.655	41.284	92.171	1.00	28.89	0

ATOM	84	OE1	GLN	14	4.726	41.428	91.363	1.00	30.84	0
ATOM	85	NE2	GLN	14	6.861	41.818	91.977	1.00	29.15	0
ATOM	88	C	GLN	14	6.088	42.519	95.515	1.00	2.00	0
ATOM	89	O	GLN	14	7.206	42.249	95.934	1.00	24.80	0
ATOM	90	N	ARG	15	5.789	43.625	94.848	1.00	15.16	0
ATOM	92	CA	ARG	15	6.776	44.638	94.552	1.00	15.16	0
ATOM	93	CB	ARG	15	6.122	45.812	93.846	1.00	8.83	0
ATOM	94	CG	ARG	15	6.530	45.981	92.388	1.00	8.83	0
ATOM	95	CD	ARG	15	5.543	46.882	91.684	1.00	8.83	0
ATOM	96	NE	ARG	15	4.195	46.322	91.761	1.00	8.83	0
ATOM	98	CZ	ARG	15	3.094	46.998	91.465	1.00	8.83	0
ATOM	99	NH1	ARG	15	3.178	48.261	91.073	1.00	9.33	0
ATOM	102	NH2	ARG	15	1.907	46.413	91.567	1.00	8.83	0
ATOM	105	C	ARG	15	7.405	45.106	95.841	1.00	15.16	0
ATOM	106	O	ARG	15	8.622	45.124	95.952	1.00	13.09	0
ATOM	107	N	LEU	16	6.575	45.462	96.820	1.00	2.00	0
ATOM	109	CA	LEU	16	7.049	45.924	98.124	1.00	2.00	0
ATOM	110	CB	LEU	16	5.853	46.215	99.033	1.00	2.00	0
ATOM	111	CG	LEU	16	4.982	47.420	98.662	1.00	2.00	0
ATOM	112	CD1	LEU	16	3.630	47.302	99.324	1.00	2.00	0
ATOM	113	CD2	LEU	16	5.664	48.707	99.056	1.00	2.00	0
ATOM	114	C	LEU	16	8.014	44.942	98.809	1.00	2.00	0
ATOM	115	O	LEU	16	9.031	45.354	99.361	1.00	2.00	0
ATOM	116	N	LEU	17	7.712	43.650	98.770	1.00	12.70	0
ATOM	118	CA	LEU	17	8.590	42.652	99.395	1.00	4.33	0
ATOM	119	CB	LEU	17	7.812	41.387	99.780	1.00	4.50	0
ATOM	120	CG	LEU	17	6.740	41.515	100.838	1.00	4.52	0
ATOM	121	CD1	LEU	17	6.338	40.159	101.302	1.00	11.14	0
ATOM	122	CD2	LEU	17	7.285	42.318	101.997	1.00	6.93	0
ATOM	123	C	LEU	17	9.796	42.225	98.548	1.00	7.39	0
ATOM	124	O	LEU	17	10.751	41.652	99.086	1.00	15.30	0
ATOM	125	N	GLU	18	9.758	42.492	97.238	1.00	65.13	0
ATOM	127	CA	GLU	18	10.847	42.104	96.329	1.00	70.48	0
ATOM	128	CB	GLU	18	10.505	42.471	94.883	1.00	89.02	0
ATOM	129	CG	GLU	18	10.769	43.929	94.547	1.00	97.06	0
ATOM	130	CD	GLU	18	10.677	44.239	93.069	1.00	39.46	0
ATOM	131	OE1	GLU	18	11.030	43.351	92.256	1.00	39.46	0
ATOM	132	OE2	GLU	18	10.265	45.375	92.727	1.00	39.46	0
ATOM	133	C	GLU	18	12.199	42.724	96.687	1.00	70.82	0
ATOM	134	O	GLU	18	13.244	42.249	96.240	1.00	88.34	0
ATOM	135	N	VAL	19	12.172	43.793	97.480	1.00	28.97	0
ATOM	137	CA	VAL	19	13.394	44.470	97.891	1.00	28.97	0
ATOM	138	CB	VAL	19	13.139	45.968	98.207	1.00	6.66	0
ATOM	139	CG1	VAL	19	12.746	46.702	96.942	1.00	6.86	0
ATOM	140	CG2	VAL	19	12.044	46.117	99.231	1.00	4.03	0
ATOM	141	C	VAL	19	14.079	43.805	99.081	1.00	28.97	0
ATOM	142	O	VAL	19	15.134	44.258	99.514	1.00	13.23	0
ATOM	143	N	ARG	20	13.490	42.736	99.615	1.00	2.00	0
ATOM	145	CA	ARG	20	14.093	42.016	100.748	1.00	2.00	0
ATOM	146	CB	ARG	20	13.242	40.812	101.142	1.00	17.66	0
ATOM	147	CG	ARG	20	12.043	41.138	101.990	1.00	16.46	0
ATOM	148	CD	ARG	20	11.192	39.899	102.195	1.00	21.30	0
ATOM	149	NE	ARG	20	12.006	38.733	102.532	1.00	18.45	0
ATOM	151	CZ	ARG	20	11.559	37.481	102.546	1.00	23.19	0
ATOM	152	NH1	ARG	20	10.288	37.232	102.249	1.00	28.11	0
ATOM	155	NH2	ARG	20	12.383	36.477	102.836	1.00	21.96	0
ATOM	158	C	ARG	20	15.480	41.521	100.333	1.00	2.00	0
ATOM	159	O	ARG	20	15.609	40.778	99.353	1.00	20.52	0
ATOM	160	N	GLY	21	16.514	41.956	101.047	1.00	61.97	0
ATOM	162	CA	GLY	21	17.863	41.527	100.718	1.00	65.49	0
ATOM	163	C	GLY	21	18.702	42.522	99.930	1.00	66.05	0
ATOM	164	O	GLY	21	19.933	42.409	99.889	1.00	13.74	0
ATOM	165	N	SER	22	18.055	43.490	99.290	1.00	19.66	0
ATOM	167	CA	SER	22	18.790	44.491	98.523	1.00	17.08	0
ATOM	168	CB	SER	22	17.874	45.159	97.481	1.00	26.61	0
ATOM	169	OG	SER	22	16.821	45.908	98.074	1.00	32.17	0
ATOM	171	C	SER	22	19.371	45.538	99.466	1.00	17.54	0
ATOM	172	O	SER	22	19.047	45.558	100.657	1.00	21.05	0

ATOM	173	N	LYS	23	20.222	46.409	98.935	1.00	53.24	0
ATOM	175	CA	LYS	23	20.828	47.458	99.740	1.00	49.50	0
ATOM	176	CB	LYS	23	21.565	48.471	98.852	1.00	94.25	0
ATOM	177	CG	LYS	23	20.639	49.422	98.085	1.00	59.71	0
ATOM	178	CD	LYS	23	21.341	50.716	97.688	1.00	94.25	0
ATOM	179	CE	LYS	23	20.346	51.775	97.214	1.00	59.77	0
ATOM	180	NZ	LYS	23	19.448	52.240	98.306	1.00	59.94	0
ATOM	184	C	LYS	23	19.739	48.190	100.528	1.00	49.47	0
ATOM	185	O	LYS	23	18.659	48.488	99.998	1.00	59.94	0
ATOM	186	N	PRO	24	19.990	48.458	101.813	1.00	37.72	0
ATOM	187	CD	PRO	24	21.185	48.148	102.614	1.00	2.00	0
ATOM	188	CA	PRO	24	18.987	49.165	102.613	1.00	36.73	0
ATOM	189	CB	PRO	24	19.618	49.217	104.004	1.00	2.00	0
ATOM	190	CG	PRO	24	21.109	49.208	103.704	1.00	2.00	0
ATOM	191	C	PRO	24	18.798	50.551	102.019	1.00	33.26	0
ATOM	192	O	PRO	24	19.752	51.325	101.938	1.00	2.00	0
ATOM	193	N	GLY	25	17.579	50.835	101.575	1.00	22.79	0
ATOM	195	CA	GLY	25	17.275	52.119	100.981	1.00	22.84	0
ATOM	196	C	GLY	25	16.653	51.904	99.624	1.00	18.00	0
ATOM	197	O	GLY	25	16.098	52.827	99.037	1.00	28.24	0
ATOM	198	N	LYS	26	16.750	50.679	99.116	1.00	2.00	0
ATOM	200	CA	LYS	26	16.174	50.351	97.817	1.00	2.00	0
ATOM	201	CB	LYS	26	16.469	48.892	97.458	1.00	45.45	0
ATOM	202	CG	LYS	26	15.931	48.437	96.110	1.00	55.13	0
ATOM	203	CD	LYS	26	16.209	49.435	94.979	1.00	59.31	0
ATOM	204	CE	LYS	26	17.694	49.644	94.691	1.00	60.93	0
ATOM	205	NZ	LYS	26	17.883	50.619	93.569	1.00	68.30	0
ATOM	209	C	LYS	26	14.674	50.624	97.856	1.00	2.00	0
ATOM	210	O	LYS	26	13.916	49.964	98.566	1.00	42.74	0
ATOM	211	N	ASN	27	14.278	51.648	97.111	1.00	2.00	0
ATOM	213	CA	ASN	27	12.894	52.086	97.027	1.00	2.00	0
ATOM	214	CB	ASN	27	12.836	53.526	96.517	1.00	50.37	0
ATOM	215	CG	ASN	27	13.257	54.525	97.563	1.00	56.29	0
ATOM	216	OD1	ASN	27	12.929	54.381	98.740	1.00	61.45	0
ATOM	217	ND2	ASN	27	13.982	55.551	97.142	1.00	59.50	0
ATOM	220	C	ASN	27	11.964	51.219	96.183	1.00	2.00	0
ATOM	221	O	ASN	27	12.384	50.256	95.540	1.00	54.11	0
ATOM	222	N	VAL	28	10.689	51.590	96.209	1.00	12.34	0
ATOM	224	CA	VAL	28	9.646	50.910	95.473	1.00	12.71	0
ATOM	225	CB	VAL	28	9.126	49.693	96.283	1.00	2.00	0
ATOM	226	CG1	VAL	28	8.777	50.111	97.684	1.00	2.00	0
ATOM	227	CG2	VAL	28	7.932	49.053	95.599	1.00	2.00	0
ATOM	228	C	VAL	28	8.549	51.935	95.145	1.00	19.22	0
ATOM	229	O	VAL	28	7.757	52.363	96.000	1.00	2.00	0
ATOM	230	N	GLN	29	8.548	52.372	93.892	1.00	26.36	0
ATOM	232	CA	GLN	29	7.586	53.365	93.424	1.00	27.97	0
ATOM	233	CB	GLN	29	8.203	54.239	92.325	1.00	11.00	0
ATOM	234	CG	GLN	29	7.479	55.543	92.080	1.00	8.47	0
ATOM	235	CD	GLN	29	7.684	56.541	93.201	1.00	11.72	0
ATOM	236	OE1	GLN	29	7.097	57.619	93.198	1.00	13.39	0
ATOM	237	NE2	GLN	29	8.525	56.195	94.159	1.00	12.03	0
ATOM	240	C	GLN	29	6.347	52.688	92.887	1.00	27.73	0
ATOM	241	O	GLN	29	6.401	51.934	91.926	1.00	8.22	0
ATOM	242	N	LEU	30	5.229	52.941	93.531	1.00	2.00	0
ATOM	244	CA	LEU	30	3.978	52.359	93.087	1.00	2.00	0
ATOM	245	CB	LEU	30	3.157	51.859	94.279	1.00	18.06	0
ATOM	246	CG	LEU	30	3.381	50.416	94.729	1.00	18.06	0
ATOM	247	CD1	LEU	30	4.857	50.152	94.928	1.00	18.06	0
ATOM	248	CD2	LEU	30	2.603	50.171	96.009	1.00	18.06	0
ATOM	249	C	LEU	30	3.223	53.441	92.348	1.00	2.00	0
ATOM	250	O	LEU	30	3.363	54.621	92.664	1.00	18.06	0
ATOM	251	N	GLN	31	2.441	53.050	91.355	1.00	75.78	0
ATOM	253	CA	GLN	31	1.679	54.026	90.599	1.00	80.15	0
ATOM	254	CB	GLN	31	0.782	53.336	89.593	1.00	2.00	0
ATOM	255	CG	GLN	31	1.448	52.204	88.883	1.00	2.00	0
ATOM	256	CD	GLN	31	0.498	51.469	87.976	1.00	2.00	0
ATOM	257	OE1	GLN	31	0.933	50.694	87.122	1.00	2.00	0
ATOM	258	NE2	GLN	31	-0.809	51.698	88.150	1.00	2.00	0

ATOM	261	C	GLN	31	0.819	54.783	91.585	1.00	79.69	0
ATOM	262	O	GLN	31	0.276	54.187	92.512	1.00	2.00	0
ATOM	263	N	GLU	32	0.716	56.091	91.380	1.00	2.00	0
ATOM	265	CA	GLU	32	-0.074	56.979	92.228	1.00	2.00	0
ATOM	266	CB	GLU	32	-0.236	58.333	91.523	1.00	57.69	0
ATOM	267	CG	GLU	32	-1.206	59.320	92.181	1.00	62.36	0
ATOM	268	CD	GLU	32	-1.652	60.426	91.226	1.00	60.46	0
ATOM	269	OE1	GLU	32	-2.596	61.176	91.570	1.00	59.61	0
ATOM	270	OE2	GLU	32	-1.059	60.543	90.128	1.00	62.85	0
ATOM	271	C	GLU	32	-1.449	56.370	92.539	1.00	2.00	0
ATOM	272	O	GLU	32	-1.875	56.341	93.695	1.00	53.86	0
ATOM	273	N	ASN	33	-2.127	55.865	91.517	1.00	6.25	0
ATOM	275	CA	ASN	33	-3.445	55.278	91.714	1.00	7.45	0
ATOM	276	CB	ASN	33	-4.134	55.026	90.364	1.00	30.19	0
ATOM	277	CG	ASN	33	-3.291	54.199	89.412	1.00	30.49	0
ATOM	278	OD1	ASN	33	-2.592	53.261	89.810	1.00	32.73	0
ATOM	279	ND2	ASN	33	-3.349	54.551	88.141	1.00	33.00	0
ATOM	282	C	ASN	33	-3.448	54.002	92.565	1.00	10.76	0
ATOM	283	O	ASN	33	-4.466	53.670	93.182	1.00	23.15	0
ATOM	284	N	GLU	34	-2.322	53.292	92.598	1.00	27.56	0
ATOM	286	CA	GLU	34	-2.217	52.081	93.402	1.00	24.54	0
ATOM	287	CB	GLU	34	-1.005	51.251	92.985	1.00	23.44	0
ATOM	288	CG	GLU	34	-1.203	50.479	91.698	1.00	22.75	0
ATOM	289	CD	GLU	34	-0.120	49.438	91.479	1.00	28.72	0
ATOM	290	OE1	GLU	34	-0.443	48.226	91.460	1.00	34.33	0
ATOM	291	OE2	GLU	34	1.055	49.834	91.330	1.00	31.11	0
ATOM	292	C	GLU	34	-2.106	52.470	94.871	1.00	25.10	0
ATOM	293	O	GLU	34	-2.797	51.923	95.716	1.00	19.23	0
ATOM	294	N	ILE	35	-1.244	53.430	95.172	1.00	14.94	0
ATOM	296	CA	ILE	35	-1.083	53.889	96.541	1.00	28.22	0
ATOM	297	CB	ILE	35	0.045	54.888	96.632	1.00	2.00	0
ATOM	298	CG2	ILE	35	0.013	55.607	97.961	1.00	2.00	0
ATOM	299	CG1	ILE	35	1.354	54.154	96.395	1.00	2.00	0
ATOM	300	CD1	ILE	35	2.554	55.045	96.414	1.00	2.00	0
ATOM	301	C	ILE	35	-2.368	54.536	97.034	1.00	13.21	0
ATOM	302	O	ILE	35	-2.794	54.302	98.172	1.00	2.00	0
ATOM	303	N	ARG	36	-2.985	55.340	96.171	1.00	2.00	0
ATOM	305	CA	ARG	36	-4.237	56.015	96.506	1.00	2.00	0
ATOM	306	CB	ARG	36	-4.578	57.082	95.446	1.00	8.06	0
ATOM	307	CG	ARG	36	-5.725	56.703	94.502	1.00	14.08	0
ATOM	308	CD	ARG	36	-6.059	57.824	93.555	1.00	20.55	0
ATOM	309	NE	ARG	36	-6.465	59.029	94.267	1.00	14.43	0
ATOM	311	CZ	ARG	36	-7.726	59.383	94.491	1.00	22.93	0
ATOM	312	NH1	ARG	36	-8.729	58.618	94.064	1.00	22.80	0
ATOM	315	NH2	ARG	36	-7.987	60.518	95.134	1.00	19.87	0
ATOM	318	C	ARG	36	-5.394	55.005	96.657	1.00	2.00	0
ATOM	319	O	ARG	36	-6.415	55.305	97.279	1.00	2.00	0
ATOM	320	N	GLY	37	-5.240	53.828	96.059	1.00	2.00	0
ATOM	322	CA	GLY	37	-6.264	52.814	96.177	1.00	2.00	0
ATOM	323	C	GLY	37	-6.118	52.251	97.575	1.00	2.00	0
ATOM	324	O	GLY	37	-7.106	52.030	98.289	1.00	2.00	0
ATOM	325	N	LEU	38	-4.864	52.039	97.975	1.00	8.88	0
ATOM	327	CA	LEU	38	-4.558	51.515	99.288	1.00	8.88	0
ATOM	328	CB	LEU	38	-3.061	51.550	99.559	1.00	2.00	0
ATOM	329	CG	LEU	38	-2.202	50.559	98.784	1.00	2.00	0
ATOM	330	CD1	LEU	38	-0.765	50.804	99.171	1.00	2.00	0
ATOM	331	CD2	LEU	38	-2.614	49.106	99.063	1.00	2.00	0
ATOM	332	C	LEU	38	-5.278	52.406	100.258	1.00	8.88	0
ATOM	333	O	LEU	38	-6.130	51.928	101.002	1.00	2.00	0
ATOM	334	N	CYS	39	-4.976	53.705	100.216	1.00	2.00	0
ATOM	336	CA	CYS	39	-5.613	54.690	101.099	1.00	2.00	0
ATOM	337	CB	CYS	39	-5.339	56.096	100.607	1.00	2.00	0
ATOM	338	SG	CYS	39	-3.719	56.686	100.830	1.00	2.00	0
ATOM	339	C	CYS	39	-7.140	54.555	101.201	1.00	2.00	0
ATOM	340	O	CYS	39	-7.708	54.580	102.296	1.00	2.00	0
ATOM	341	N	LEU	40	-7.793	54.412	100.053	1.00	2.00	0
ATOM	343	CA	LEU	40	-9.233	54.330	99.999	1.00	2.00	0
ATOM	344	CB	LEU	40	-9.735	54.704	98.599	1.00	2.00	0

ATOM	345	CG	LEU	40	-10.127	56.184	98.419	1.00	2.00	0
ATOM	346	CD1	LEU	40	-9.020	57.095	98.939	1.00	2.00	0
ATOM	347	CD2	LEU	40	-10.401	56.484	96.960	1.00	2.00	0
ATOM	348	C	LEU	40	-9.817	53.014	100.426	1.00	2.00	0
ATOM	349	O	LEU	40	-10.853	52.987	101.071	1.00	2.00	0
ATOM	350	N	LYS	41	-9.174	51.916	100.081	1.00	7.31	0
ATOM	352	CA	LYS	41	-9.721	50.630	100.468	1.00	7.31	0
ATOM	353	CB	LYS	41	-9.123	49.517	99.598	1.00	2.00	0
ATOM	354	CG	LYS	41	-9.685	48.157	99.884	1.00	2.00	0
ATOM	355	CD	LYS	41	-11.188	48.216	99.923	1.00	2.00	0
ATOM	356	CE	LYS	41	-11.746	46.968	100.560	1.00	2.00	0
ATOM	357	NZ	LYS	41	-11.198	45.721	99.910	1.00	2.00	0
ATOM	361	C	LYS	41	-9.475	50.376	101.963	1.00	7.31	0
ATOM	362	O	LYS	41	-10.375	49.934	102.674	1.00	2.00	0
ATOM	363	N	SER	42	-8.266	50.666	102.440	1.00	3.34	0
ATOM	365	CA	SER	42	-7.935	50.477	103.844	1.00	3.34	0
ATOM	366	CB	SER	42	-6.496	50.854	104.094	1.00	2.00	0
ATOM	367	OG	SER	42	-6.315	52.215	103.766	1.00	2.00	0
ATOM	369	C	SER	42	-8.844	51.398	104.650	1.00	7.34	0
ATOM	370	O	SER	42	-9.504	50.955	105.600	1.00	2.00	0
ATOM	371	N	ARG	43	-8.906	52.671	104.247	1.00	2.00	0
ATOM	373	CA	ARG	43	-9.746	53.650	104.928	1.00	2.00	0
ATOM	374	CB	ARG	43	-9.856	54.946	104.135	1.00	2.00	0
ATOM	375	CG	ARG	43	-10.530	56.063	104.917	1.00	2.00	0
ATOM	376	CD	ARG	43	-11.541	56.826	104.097	1.00	2.00	0
ATOM	377	NE	ARG	43	-11.803	58.137	104.679	1.00	2.00	0
ATOM	379	CZ	ARG	43	-13.010	58.603	105.005	1.00	2.00	0
ATOM	380	NH1	ARG	43	-14.112	57.877	104.826	1.00	2.00	0
ATOM	383	NH2	ARG	43	-13.120	59.827	105.502	1.00	2.00	0
ATOM	386	C	ARG	43	-11.136	53.103	105.104	1.00	2.00	0
ATOM	387	O	ARG	43	-11.800	53.385	106.083	1.00	2.00	0
ATOM	388	N	GLU	44	-11.574	52.321	104.130	1.00	19.11	0
ATOM	390	CA	GLU	44	-12.901	51.727	104.146	1.00	19.41	0
ATOM	391	CB	GLU	44	-13.179	51.107	102.776	1.00	23.41	0
ATOM	392	CG	GLU	44	-14.599	50.695	102.542	1.00	34.12	0
ATOM	393	CD	GLU	44	-14.711	49.574	101.532	1.00	38.72	0
ATOM	394	OE1	GLU	44	-15.634	49.626	100.699	1.00	43.51	0
ATOM	395	OE2	GLU	44	-13.886	48.639	101.576	1.00	35.90	0
ATOM	396	C	GLU	44	-12.987	50.674	105.260	1.00	20.56	0
ATOM	397	O	GLU	44	-13.967	50.622	106.007	1.00	24.61	0
ATOM	398	N	ILE	45	-11.945	49.857	105.379	1.00	8.30	0
ATOM	400	CA	ILE	45	-11.896	48.811	106.384	1.00	8.30	0
ATOM	401	CB	ILE	45	-10.720	47.876	106.133	1.00	2.00	0
ATOM	402	CG2	ILE	45	-10.795	46.678	107.049	1.00	2.00	0
ATOM	403	CG1	ILE	45	-10.774	47.382	104.698	1.00	2.00	0
ATOM	404	CD1	ILE	45	-9.559	46.593	104.285	1.00	2.00	0
ATOM	405	C	ILE	45	-11.775	49.401	107.784	1.00	8.30	0
ATOM	406	O	ILE	45	-12.249	48.819	108.756	1.00	2.00	0
ATOM	407	N	PHE	46	-11.134	50.550	107.905	1.00	2.00	0
ATOM	409	CA	PHE	46	-11.013	51.154	109.214	1.00	2.00	0
ATOM	410	CB	PHE	46	-10.076	52.352	109.176	1.00	2.00	0
ATOM	411	CG	PHE	46	-8.665	51.992	108.843	1.00	2.00	0
ATOM	412	CD1	PHE	46	-7.829	52.906	108.223	1.00	2.00	0
ATOM	413	CD2	PHE	46	-8.168	50.726	109.151	1.00	2.00	0
ATOM	414	CE1	PHE	46	-6.516	52.558	107.915	1.00	2.00	0
ATOM	415	CE2	PHE	46	-6.859	50.375	108.845	1.00	2.00	0
ATOM	416	CZ	PHE	46	-6.027	51.289	108.227	1.00	2.00	0
ATOM	417	C	PHE	46	-12.396	51.561	109.686	1.00	2.00	0
ATOM	418	O	PHE	46	-12.840	51.109	110.731	1.00	2.00	0
ATOM	419	N	LEU	47	-13.106	52.358	108.896	1.00	2.00	0
ATOM	421	CA	LEU	47	-14.441	52.807	109.277	1.00	2.00	0
ATOM	422	CB	LEU	47	-15.043	53.705	108.190	1.00	2.00	0
ATOM	423	CG	LEU	47	-14.641	55.181	108.110	1.00	2.00	0
ATOM	424	CD1	LEU	47	-14.094	55.641	109.462	1.00	2.00	0
ATOM	425	CD2	LEU	47	-13.619	55.397	107.030	1.00	2.00	0
ATOM	426	C	LEU	47	-15.424	51.677	109.578	1.00	2.00	0
ATOM	427	O	LEU	47	-16.432	51.905	110.243	1.00	2.00	0
ATOM	428	N	SER	48	-15.145	50.469	109.091	1.00	2.00	0

ATOM	430	CA	SER	48	-16.037	49.339	109.305	1.00	2.00	0
ATOM	431	CB	SER	48	-16.121	48.483	108.039	1.00	23.35	0
ATOM	432	OG	SER	48	-14.844	48.045	107.622	1.00	30.63	0
ATOM	434	C	SER	48	-15.624	48.473	110.482	1.00	2.00	0
ATOM	435	O	SER	48	-16.184	47.390	110.700	1.00	28.70	0
ATOM	436	N	GLN	49	-14.627	48.922	111.225	1.00	61.72	0
ATOM	438	CA	GLN	49	-14.175	48.193	112.394	1.00	63.25	0
ATOM	439	CB	GLN	49	-12.763	47.645	112.173	1.00	13.32	0
ATOM	440	CG	GLN	49	-12.668	46.511	111.146	1.00	7.00	0
ATOM	441	CD	GLN	49	-11.246	45.952	110.995	1.00	8.88	0
ATOM	442	OE1	GLN	49	-10.251	46.640	111.258	1.00	9.23	0
ATOM	443	NE2	GLN	49	-11.151	44.700	110.573	1.00	7.45	0
ATOM	446	C	GLN	49	-14.210	49.205	113.540	1.00	63.04	0
ATOM	447	O	GLN	49	-13.864	50.373	113.357	1.00	14.61	0
ATOM	448	N	PRO	50	-14.645	48.778	114.734	1.00	34.58	0
ATOM	449	CD	PRO	50	-14.967	47.399	115.118	1.00	4.85	0
ATOM	450	CA	PRO	50	-14.728	49.657	115.901	1.00	34.58	0
ATOM	451	CB	PRO	50	-15.037	48.678	117.032	1.00	2.00	0
ATOM	452	CG	PRO	50	-14.496	47.365	116.531	1.00	2.00	0
ATOM	453	C	PRO	50	-13.459	50.468	116.164	1.00	34.58	0
ATOM	454	O	PRO	50	-12.356	50.002	115.884	1.00	2.95	0
ATOM	455	N	ILE	51	-13.626	51.673	116.708	1.00	2.00	0
ATOM	457	CA	ILE	51	-12.499	52.550	117.015	1.00	2.00	0
ATOM	458	CB	ILE	51	-13.001	53.975	117.318	1.00	2.00	0
ATOM	459	CG2	ILE	51	-13.642	54.035	118.673	1.00	2.00	0
ATOM	460	CG1	ILE	51	-11.850	54.958	117.295	1.00	2.00	0
ATOM	461	CD1	ILE	51	-12.328	56.370	117.351	1.00	2.00	0
ATOM	462	C	ILE	51	-11.650	51.996	118.172	1.00	2.00	0
ATOM	463	O	ILE	51	-10.456	52.303	118.283	1.00	2.00	0
ATOM	464	N	LEU	52	-12.284	51.187	119.028	1.00	2.00	0
ATOM	466	CA	LEU	52	-11.622	50.522	120.159	1.00	2.00	0
ATOM	467	CB	LEU	52	-12.391	50.746	121.473	1.00	2.00	0
ATOM	468	CG	LEU	52	-11.655	50.518	122.808	1.00	2.00	0
ATOM	469	CD1	LEU	52	-12.559	50.899	123.944	1.00	2.00	0
ATOM	470	CD2	LEU	52	-11.233	49.085	122.973	1.00	2.00	0
ATOM	471	C	LEU	52	-11.660	49.033	119.770	1.00	2.00	0
ATOM	472	O	LEU	52	-12.652	48.331	120.006	1.00	2.00	0
ATOM	473	N	LEU	53	-10.584	48.576	119.136	1.00	2.00	0
ATOM	475	CA	LEU	53	-10.464	47.204	118.667	1.00	2.00	0
ATOM	476	CB	LEU	53	-9.066	46.982	118.069	1.00	2.00	0
ATOM	477	CG	LEU	53	-8.802	47.038	116.555	1.00	2.00	0
ATOM	478	CD1	LEU	53	-9.835	47.889	115.810	1.00	2.00	0
ATOM	479	CD2	LEU	53	-7.401	47.550	116.353	1.00	2.00	0
ATOM	480	C	LEU	53	-10.686	46.230	119.792	1.00	2.00	0
ATOM	481	O	LEU	53	-10.365	46.522	120.937	1.00	2.00	0
ATOM	482	N	GLU	54	-11.251	45.076	119.472	1.00	19.77	0
ATOM	484	CA	GLU	54	-11.465	44.049	120.474	1.00	20.13	0
ATOM	485	CB	GLU	54	-12.955	43.809	120.714	1.00	56.32	0
ATOM	486	CG	GLU	54	-13.244	43.362	122.135	1.00	66.19	0
ATOM	487	CD	GLU	54	-14.668	42.873	122.346	1.00	69.64	0
ATOM	488	OE1	GLU	54	-15.613	43.627	122.024	1.00	78.06	0
ATOM	489	OE2	GLU	54	-14.839	41.734	122.848	1.00	73.27	0
ATOM	490	C	GLU	54	-10.798	42.820	119.882	1.00	19.77	0
ATOM	491	O	GLU	54	-11.451	41.949	119.313	1.00	48.57	0
ATOM	492	N	LEU	55	-9.473	42.800	119.974	1.00	2.00	0
ATOM	494	CA	LEU	55	-8.666	41.712	119.452	1.00	2.00	0
ATOM	495	CB	LEU	55	-7.245	42.188	119.176	1.00	2.00	0
ATOM	496	CG	LEU	55	-7.148	43.458	118.336	1.00	2.00	0
ATOM	497	CD1	LEU	55	-5.695	43.728	117.961	1.00	2.00	0
ATOM	498	CD2	LEU	55	-8.024	43.298	117.108	1.00	2.00	0
ATOM	499	C	LEU	55	-8.624	40.586	120.456	1.00	2.00	0
ATOM	500	O	LEU	55	-8.724	40.807	121.664	1.00	10.45	0
ATOM	501	N	GLU	56	-8.448	39.374	119.961	1.00	2.00	0
ATOM	503	CA	GLU	56	-8.407	38.224	120.826	1.00	2.00	0
ATOM	504	CB	GLU	56	-9.741	37.467	120.729	1.00	18.79	0
ATOM	505	CG	GLU	56	-10.989	38.283	121.171	1.00	30.34	0
ATOM	506	CD	GLU	56	-11.012	38.677	122.658	1.00	42.94	0
ATOM	507	OE1	GLU	56	-11.188	37.789	123.526	1.00	44.70	0

ATOM	508	OE2	GLU	56	-10.872	39.882	122.955	1.00	47.48	0
ATOM	509	C	GLU	56	-7.244	37.343	120.393	1.00	2.00	0
ATOM	510	O	GLU	56	-6.292	37.839	119.800	1.00	3.40	0
ATOM	511	N	ALA	57	-7.312	36.062	120.765	1.00	65.90	0
ATOM	513	CA	ALA	57	-6.336	35.026	120.405	1.00	62.88	0
ATOM	514	CB	ALA	57	-6.750	34.434	119.039	1.00	26.61	0
ATOM	515	C	ALA	57	-4.867	35.474	120.387	1.00	68.03	0
ATOM	516	O	ALA	57	-4.543	36.519	120.932	1.00	14.05	0
ATOM	517	N	PRO	58	-3.951	34.632	119.857	1.00	2.00	0
ATOM	518	CD	PRO	58	-4.109	33.203	119.533	1.00	9.23	0
ATOM	519	CA	PRO	58	-2.526	34.988	119.782	1.00	2.00	0
ATOM	520	CB	PRO	58	-1.852	33.645	119.501	1.00	9.23	0
ATOM	521	CG	PRO	58	-2.881	32.926	118.711	1.00	9.49	0
ATOM	522	C	PRO	58	-2.176	36.002	118.672	1.00	2.00	0
ATOM	523	O	PRO	58	-2.688	35.901	117.540	1.00	12.29	0
ATOM	524	N	LEU	59	-1.284	36.947	118.975	1.00	17.05	0
ATOM	526	CA	LEU	59	-0.856	37.944	117.989	1.00	17.05	0
ATOM	527	CB	LEU	59	-1.862	39.100	117.895	1.00	2.00	0
ATOM	528	CG	LEU	59	-1.842	40.166	118.993	1.00	2.00	0
ATOM	529	CD1	LEU	59	-2.880	41.252	118.706	1.00	2.00	0
ATOM	530	CD2	LEU	59	-2.117	39.498	120.339	1.00	2.00	0
ATOM	531	C	LEU	59	0.510	38.501	118.351	1.00	17.05	0
ATOM	532	O	LEU	59	1.030	38.229	119.429	1.00	2.00	0
ATOM	533	N	LYS	60	1.103	39.259	117.438	1.00	21.64	0
ATOM	535	CA	LYS	60	2.399	39.872	117.688	1.00	21.64	0
ATOM	536	CB	LYS	60	3.358	39.655	116.513	1.00	10.44	0
ATOM	537	CG	LYS	60	3.185	38.327	115.768	1.00	11.70	0
ATOM	538	CD	LYS	60	3.556	37.101	116.608	1.00	12.19	0
ATOM	539	CE	LYS	60	5.034	36.783	116.544	1.00	8.37	0
ATOM	540	NZ	LYS	60	5.824	37.927	117.066	1.00	8.37	0
ATOM	544	C	LYS	60	2.063	41.353	117.804	1.00	21.64	0
ATOM	545	O	LYS	60	1.142	41.832	117.128	1.00	13.47	0
ATOM	546	N	ILE	61	2.757	42.072	118.680	1.00	20.60	0
ATOM	548	CA	ILE	61	2.499	43.496	118.822	1.00	22.32	0
ATOM	549	CB	ILE	61	2.032	43.859	120.240	1.00	2.00	0
ATOM	550	CG2	ILE	61	1.485	45.288	120.239	1.00	2.00	0
ATOM	551	CG1	ILE	61	0.940	42.881	120.702	1.00	2.00	0
ATOM	552	CD1	ILE	61	0.019	43.422	121.783	1.00	2.00	0
ATOM	553	C	ILE	61	3.791	44.220	118.494	1.00	23.52	0
ATOM	554	O	ILE	61	4.862	43.752	118.868	1.00	2.00	0
ATOM	555	N	CYS	62	3.698	45.341	117.787	1.00	2.00	0
ATOM	557	CA	CYS	62	4.874	46.095	117.393	1.00	2.00	0
ATOM	558	CB	CYS	62	5.147	45.925	115.895	1.00	11.47	0
ATOM	559	SG	CYS	62	5.439	44.252	115.266	1.00	11.47	0
ATOM	560	C	CYS	62	4.607	47.560	117.658	1.00	2.00	0
ATOM	561	O	CYS	62	3.451	47.957	117.751	1.00	11.47	0
ATOM	562	N	GLY	63	5.662	48.367	117.739	1.00	2.00	0
ATOM	564	CA	GLY	63	5.507	49.789	117.971	1.00	2.00	0
ATOM	565	C	GLY	63	6.548	50.610	117.222	1.00	2.00	0
ATOM	566	O	GLY	63	7.624	50.109	116.897	1.00	11.39	0
ATOM	567	N	ASP	64	6.216	51.870	116.959	1.00	2.00	0
ATOM	569	CA	ASP	64	7.068	52.834	116.255	1.00	3.88	0
ATOM	570	CB	ASP	64	7.805	53.721	117.245	1.00	6.62	0
ATOM	571	CG	ASP	64	6.873	54.589	118.025	1.00	6.62	0
ATOM	572	OD1	ASP	64	5.996	54.019	118.708	1.00	12.70	0
ATOM	573	OD2	ASP	64	7.003	55.829	117.946	1.00	12.70	0
ATOM	574	C	ASP	64	8.064	52.362	115.221	1.00	14.37	0
ATOM	575	O	ASP	64	9.221	52.080	115.557	1.00	8.57	0
ATOM	576	N	ILE	65	7.619	52.326	113.963	1.00	5.19	0
ATOM	578	CA	ILE	65	8.471	51.924	112.849	1.00	3.07	0
ATOM	579	CB	ILE	65	7.663	51.310	111.672	1.00	2.00	0
ATOM	580	CG2	ILE	65	8.609	50.903	110.535	1.00	2.00	0
ATOM	581	CG1	ILE	65	6.871	50.095	112.151	1.00	2.00	0
ATOM	582	CD1	ILE	65	7.723	49.023	112.763	1.00	2.00	0
ATOM	583	C	ILE	65	9.185	53.177	112.357	1.00	2.24	0
ATOM	584	O	ILE	65	10.379	53.148	112.101	1.00	2.00	0
ATOM	585	N	HIS	66	8.451	54.276	112.235	1.00	2.00	0
ATOM	587	CA	HIS	66	9.022	55.536	111.776	1.00	2.00	0

ATOM	588	C	HIS	66	9.847	55.525	110.502	1.00	2.00	0
ATOM	589	O	HIS	66	11.042	55.818	110.539	1.00	12.38	0
ATOM	590	CB	HIS	66	9.846	56.182	112.881	1.00	8.25	0
ATOM	591	CG	HIS	66	9.040	57.046	113.782	1.00	8.25	0
ATOM	592	ND1	HIS	66	8.104	57.949	113.337	1.00	8.25	0
ATOM	594	CD2	HIS	66	9.001	57.109	115.133	1.00	8.25	0
ATOM	595	NE2	HIS	66	8.042	58.043	115.526	1.00	8.25	0
ATOM	596	CE1	HIS	66	7.536	58.516	114.399	1.00	8.25	0
ATOM	597	N	GLY	67	9.197	55.195	109.385	1.00	11.52	0
ATOM	599	CA	GLY	67	9.835	55.174	108.078	1.00	11.52	0
ATOM	600	C	GLY	67	11.029	54.266	107.868	1.00	11.52	0
ATOM	601	O	GLY	67	11.782	54.462	106.915	1.00	81.94	0
ATOM	602	N	GLN	68	11.214	53.272	108.730	1.00	18.96	0
ATOM	604	CA	GLN	68	12.353	52.364	108.602	1.00	20.32	0
ATOM	605	CB	GLN	68	13.007	52.139	109.957	1.00	6.39	0
ATOM	606	CG	GLN	68	13.261	53.407	110.711	1.00	4.06	0
ATOM	607	CD	GLN	68	14.315	53.239	111.757	1.00	7.01	0
ATOM	608	OE1	GLN	68	15.013	54.197	112.111	1.00	8.21	0
ATOM	609	NE2	GLN	68	14.453	52.020	112.270	1.00	5.84	0
ATOM	612	C	GLN	68	11.916	51.039	108.010	1.00	18.72	0
ATOM	613	O	GLN	68	12.018	49.975	108.634	1.00	10.73	0
ATOM	614	N	TYR	69	11.450	51.119	106.777	1.00	5.70	0
ATOM	616	CA	TYR	69	10.959	49.970	106.054	1.00	5.52	0
ATOM	617	CB	TYR	69	10.807	50.313	104.587	1.00	2.00	0
ATOM	618	CG	TYR	69	9.988	49.322	103.841	1.00	2.00	0
ATOM	619	CD1	TYR	69	8.658	49.099	104.187	1.00	2.00	0
ATOM	620	CE1	TYR	69	7.873	48.194	103.477	1.00	2.00	0
ATOM	621	CD2	TYR	69	10.526	48.611	102.762	1.00	2.00	0
ATOM	622	CE2	TYR	69	9.751	47.701	102.038	1.00	2.00	0
ATOM	623	CZ	TYR	69	8.431	47.506	102.408	1.00	2.00	0
ATOM	624	OH	TYR	69	7.656	46.632	101.715	1.00	2.00	0
ATOM	626	C	TYR	69	11.815	48.730	106.188	1.00	8.52	0
ATOM	627	O	TYR	69	11.284	47.641	106.393	1.00	2.00	0
ATOM	628	N	TYR	70	13.132	48.877	106.093	1.00	2.00	0
ATOM	630	CA	TYR	70	13.992	47.703	106.186	1.00	2.00	0
ATOM	631	CB	TYR	70	15.420	48.031	105.741	1.00	64.80	0
ATOM	632	CG	TYR	70	15.533	47.964	104.231	1.00	70.91	0
ATOM	633	CD1	TYR	70	15.026	48.993	103.431	1.00	73.06	0
ATOM	634	CE1	TYR	70	15.082	48.924	102.041	1.00	68.38	0
ATOM	635	CD2	TYR	70	16.107	46.857	103.597	1.00	73.86	0
ATOM	636	CE2	TYR	70	16.171	46.780	102.200	1.00	70.94	0
ATOM	637	CZ	TYR	70	15.654	47.820	101.433	1.00	72.52	0
ATOM	638	OH	TYR	70	15.712	47.779	100.062	1.00	70.35	0
ATOM	640	C	TYR	70	13.943	47.007	107.538	1.00	2.00	0
ATOM	641	O	TYR	70	13.967	45.771	107.610	1.00	64.08	0
ATOM	642	N	ASP	71	13.821	47.789	108.608	1.00	7.87	0
ATOM	644	CA	ASP	71	13.728	47.203	109.927	1.00	6.73	0
ATOM	645	CB	ASP	71	14.030	48.242	110.998	1.00	14.88	0
ATOM	646	CG	ASP	71	15.514	48.600	111.054	1.00	25.87	0
ATOM	647	OD1	ASP	71	15.826	49.778	111.293	1.00	24.58	0
ATOM	648	OD2	ASP	71	16.375	47.714	110.861	1.00	21.52	0
ATOM	649	C	ASP	71	12.331	46.622	110.051	1.00	6.73	0
ATOM	650	O	ASP	71	12.116	45.697	110.826	1.00	14.14	0
ATOM	651	N	LEU	72	11.399	47.148	109.250	1.00	2.00	0
ATOM	653	CA	LEU	72	10.015	46.654	109.208	1.00	2.00	0
ATOM	654	CB	LEU	72	9.094	47.613	108.456	1.00	2.00	0
ATOM	655	CG	LEU	72	7.771	46.946	108.067	1.00	2.00	0
ATOM	656	CD1	LEU	72	7.025	46.562	109.342	1.00	2.00	0
ATOM	657	CD2	LEU	72	6.935	47.867	107.208	1.00	2.00	0
ATOM	658	C	LEU	72	10.014	45.320	108.476	1.00	2.00	0
ATOM	659	O	LEU	72	9.259	44.401	108.814	1.00	2.00	0
ATOM	660	N	LEU	73	10.848	45.231	107.449	1.00	44.35	0
ATOM	662	CA	LEU	73	10.968	44.005	106.693	1.00	42.59	0
ATOM	663	CB	LEU	73	11.846	44.218	105.460	1.00	2.00	0
ATOM	664	CG	LEU	73	11.248	44.759	104.160	1.00	2.00	0
ATOM	665	CD1	LEU	73	12.324	44.728	103.101	1.00	2.00	0
ATOM	666	CD2	LEU	73	10.052	43.920	103.725	1.00	2.00	0
ATOM	667	C	LEU	73	11.603	42.978	107.629	1.00	42.42	0

ATOM	668	O	LEU	73	11.059	41.890	107.817	1.00	2.00	0
ATOM	669	N	ARG	74	12.729	43.354	108.241	1.00	2.00	0
ATOM	671	CA	ARG	74	13.462	42.494	109.179	1.00	2.00	0
ATOM	672	CB	ARG	74	14.591	43.285	109.840	1.00	31.22	0
ATOM	673	CG	ARG	74	15.809	43.478	108.958	1.00	31.18	0
ATOM	674	CD	ARG	74	16.944	44.146	109.710	1.00	37.63	0
ATOM	675	NE	ARG	74	17.250	43.459	110.960	1.00	37.44	0
ATOM	677	CZ	ARG	74	17.210	44.041	112.157	1.00	41.10	0
ATOM	678	NH1	ARG	74	16.888	45.327	112.265	1.00	39.99	0
ATOM	681	NH2	ARG	74	17.476	43.339	113.254	1.00	39.22	0
ATOM	684	C	ARG	74	12.569	41.896	110.259	1.00	2.00	0
ATOM	685	O	ARG	74	12.621	40.703	110.544	1.00	29.18	0
ATOM	686	N	LEU	75	11.747	42.742	110.853	1.00	2.00	0
ATOM	688	CA	LEU	75	10.818	42.331	111.901	1.00	2.00	0
ATOM	689	CB	LEU	75	10.069	43.580	112.407	1.00	3.53	0
ATOM	690	CG	LEU	75	8.704	43.654	113.091	1.00	3.53	0
ATOM	691	CD1	LEU	75	8.554	45.074	113.606	1.00	3.53	0
ATOM	692	CD2	LEU	75	7.561	43.337	112.138	1.00	3.53	0
ATOM	693	C	LEU	75	9.850	41.279	111.384	1.00	2.00	0
ATOM	694	O	LEU	75	9.594	40.284	112.043	1.00	3.53	0
ATOM	695	N	PHE	76	9.325	41.514	110.190	1.00	2.00	0
ATOM	697	CA	PHE	76	8.382	40.604	109.573	1.00	2.00	0
ATOM	698	CB	PHE	76	7.883	41.173	108.255	1.00	2.00	0
ATOM	699	CG	PHE	76	6.626	41.966	108.382	1.00	2.00	0
ATOM	700	CD1	PHE	76	6.447	43.124	107.642	1.00	2.00	0
ATOM	701	CD2	PHE	76	5.616	41.550	109.240	1.00	2.00	0
ATOM	702	CE1	PHE	76	5.277	43.852	107.753	1.00	2.00	0
ATOM	703	CE2	PHE	76	4.447	42.270	109.358	1.00	2.00	0
ATOM	704	CZ	PHE	76	4.272	43.423	108.615	1.00	2.00	0
ATOM	705	C	PHE	76	9.016	39.271	109.322	1.00	2.00	0
ATOM	706	O	PHE	76	8.339	38.260	109.363	1.00	2.00	0
ATOM	707	N	GLU	77	10.316	39.283	109.043	1.00	2.00	0
ATOM	709	CA	GLU	77	11.080	38.065	108.789	1.00	2.00	0
ATOM	710	CB	GLU	77	12.436	38.409	108.191	1.00	84.85	0
ATOM	711	CG	GLU	77	12.331	39.117	106.861	1.00	89.26	0
ATOM	712	CD	GLU	77	13.651	39.690	106.391	1.00	98.60	0
ATOM	713	OE1	GLU	77	13.627	40.493	105.434	1.00	98.04	0
ATOM	714	OE2	GLU	77	14.709	39.345	106.973	1.00	0.97	0
ATOM	715	C	GLU	77	11.262	37.316	110.100	1.00	2.00	0
ATOM	716	O	GLU	77	11.469	36.103	110.099	1.00	80.75	0
ATOM	717	N	TYR	78	11.182	38.045	111.216	1.00	15.29	0
ATOM	719	CA	TYR	78	11.325	37.449	112.538	1.00	15.29	0
ATOM	720	CB	TYR	78	11.945	38.455	113.514	1.00	67.13	0
ATOM	721	CG	TYR	78	12.459	37.828	114.796	1.00	69.14	0
ATOM	722	CD1	TYR	78	11.822	36.717	115.368	1.00	76.95	0
ATOM	723	CE1	TYR	78	12.278	36.142	116.548	1.00	77.96	0
ATOM	724	CD2	TYR	78	13.577	38.346	115.446	1.00	75.81	0
ATOM	725	CE2	TYR	78	14.044	37.775	116.638	1.00	77.77	0
ATOM	726	CZ	TYR	78	13.387	36.673	117.181	1.00	77.18	0
ATOM	727	OH	TYR	78	13.826	36.115	118.365	1.00	87.14	0
ATOM	729	C	TYR	78	9.967	36.964	113.053	1.00	15.29	0
ATOM	730	O	TYR	78	9.811	35.796	113.403	1.00	62.78	0
ATOM	731	N	GLY	79	8.992	37.863	113.117	1.00	2.00	0
ATOM	733	CA	GLY	79	7.675	37.485	113.582	1.00	2.00	0
ATOM	734	C	GLY	79	6.977	36.532	112.629	1.00	2.00	0
ATOM	735	O	GLY	79	6.226	35.649	113.052	1.00	34.11	0
ATOM	736	N	GLY	80	7.237	36.699	111.338	1.00	49.23	0
ATOM	738	CA	GLY	80	6.601	35.870	110.330	1.00	48.34	0
ATOM	739	C	GLY	80	5.699	36.782	109.520	1.00	47.91	0
ATOM	740	O	GLY	80	4.955	37.572	110.097	1.00	15.83	0
ATOM	741	N	PHE	81	5.759	36.692	108.193	1.00	2.00	0
ATOM	743	CA	PHE	81	4.948	37.558	107.343	1.00	2.00	0
ATOM	744	CB	PHE	81	5.386	37.403	105.880	1.00	2.00	0
ATOM	745	CG	PHE	81	6.673	38.134	105.556	1.00	2.00	0
ATOM	746	CD1	PHE	81	7.899	37.506	105.685	1.00	2.00	0
ATOM	747	CD2	PHE	81	6.652	39.467	105.139	1.00	2.00	0
ATOM	748	CE1	PHE	81	9.082	38.193	105.405	1.00	2.00	0
ATOM	749	CE2	PHE	81	7.829	40.154	104.859	1.00	2.00	0

ATOM	750	CZ	PHE	81	9.044	39.517	104.992	1.00	2.00	0
ATOM	751	C	PHE	81	3.428	37.380	107.548	1.00	2.00	0
ATOM	752	O	PHE	81	2.918	36.257	107.636	1.00	2.00	0
ATOM	753	N	PRO	82	2.694	38.505	107.618	1.00	2.00	0
ATOM	754	CD	PRO	82	3.317	39.807	107.337	1.00	21.23	0
ATOM	755	CA	PRO	82	1.261	38.702	107.820	1.00	2.00	0
ATOM	756	CB	PRO	82	0.996	39.979	107.079	1.00	20.78	0
ATOM	757	CG	PRO	82	2.144	40.765	107.502	1.00	22.98	0
ATOM	758	C	PRO	82	0.273	37.623	107.490	1.00	2.00	0
ATOM	759	O	PRO	82	-0.761	37.529	108.161	1.00	36.87	0
ATOM	760	N	PRO	83	0.501	36.841	106.423	1.00	27.66	0
ATOM	761	CD	PRO	83	1.439	36.880	105.290	1.00	2.85	0
ATOM	762	CA	PRO	83	-0.514	35.812	106.201	1.00	30.55	0
ATOM	763	CB	PRO	83	0.089	34.958	105.083	1.00	5.44	0
ATOM	764	CG	PRO	83	1.550	35.427	104.971	1.00	10.08	0
ATOM	765	C	PRO	83	-0.791	34.990	107.460	1.00	24.53	0
ATOM	766	O	PRO	83	-1.947	34.863	107.882	1.00	5.06	0
ATOM	767	N	GLU	84	0.284	34.504	108.080	1.00	63.06	0
ATOM	769	CA	GLU	84	0.190	33.665	109.268	1.00	65.66	0
ATOM	770	CB	GLU	84	1.448	32.797	109.382	1.00	61.87	0
ATOM	771	CG	GLU	84	1.194	31.402	109.979	1.00	75.07	0
ATOM	772	CD	GLU	84	0.401	30.452	109.056	1.00	79.88	0
ATOM	773	OE1	GLU	84	1.015	29.508	108.504	1.00	76.25	0
ATOM	774	OE2	GLU	84	-0.832	30.635	108.891	1.00	74.31	0
ATOM	775	C	GLU	84	-0.066	34.394	110.588	1.00	66.47	0
ATOM	776	O	GLU	84	-1.194	34.406	111.085	1.00	61.22	0
ATOM	777	N	SER	85	0.984	34.978	111.161	1.00	66.52	0
ATOM	779	CA	SER	85	0.882	35.691	112.431	1.00	64.76	0
ATOM	780	CB	SER	85	2.266	36.145	112.900	1.00	2.00	0
ATOM	781	OG	SER	85	3.198	35.078	112.871	1.00	2.00	0
ATOM	783	C	SER	85	-0.013	36.917	112.349	1.00	62.83	0
ATOM	784	O	SER	85	-0.005	37.633	111.341	1.00	2.00	0
ATOM	785	N	ASN	86	-0.785	37.146	113.412	1.00	2.00	0
ATOM	787	CA	ASN	86	-1.647	38.321	113.490	1.00	2.00	0
ATOM	788	CB	ASN	86	-2.747	38.123	114.520	1.00	2.00	0
ATOM	789	CG	ASN	86	-3.887	37.283	113.994	1.00	10.84	0
ATOM	790	OD1	ASN	86	-3.763	36.629	112.957	1.00	12.15	0
ATOM	791	ND2	ASN	86	-5.017	37.300	114.705	1.00	6.45	0
ATOM	794	C	ASN	86	-0.742	39.467	113.912	1.00	2.00	0
ATOM	795	O	ASN	86	0.363	39.229	114.423	1.00	2.00	0
ATOM	796	N	TYR	87	-1.183	40.703	113.723	1.00	2.00	0
ATOM	798	CA	TYR	87	-0.337	41.830	114.081	1.00	2.00	0
ATOM	799	CB	TYR	87	0.529	42.253	112.870	1.00	2.00	0
ATOM	800	CG	TYR	87	1.802	41.448	112.684	1.00	2.00	0
ATOM	801	CD1	TYR	87	1.879	40.421	111.749	1.00	2.00	0
ATOM	802	CE1	TYR	87	3.039	39.689	111.598	1.00	2.00	0
ATOM	803	CD2	TYR	87	2.930	41.714	113.458	1.00	2.00	0
ATOM	804	CE2	TYR	87	4.080	40.991	113.313	1.00	2.00	0
ATOM	805	CZ	TYR	87	4.127	39.986	112.384	1.00	2.00	0
ATOM	806	OH	TYR	87	5.280	39.281	112.259	1.00	2.00	0
ATOM	808	C	TYR	87	-1.104	43.029	114.588	1.00	2.00	0
ATOM	809	O	TYR	87	-2.264	43.238	114.216	1.00	2.00	0
ATOM	810	N	LEU	88	-0.440	43.810	115.435	1.00	2.00	0
ATOM	812	CA	LEU	88	-1.015	45.026	115.987	1.00	2.00	0
ATOM	813	CB	LEU	88	-1.615	44.766	117.375	1.00	2.00	0
ATOM	814	CG	LEU	88	-2.364	45.917	118.062	1.00	2.00	0
ATOM	815	CD1	LEU	88	-3.657	46.225	117.348	1.00	2.00	0
ATOM	816	CD2	LEU	88	-2.675	45.551	119.493	1.00	2.00	0
ATOM	817	C	LEU	88	0.119	46.034	116.084	1.00	2.00	0
ATOM	818	O	LEU	88	1.082	45.814	116.814	1.00	2.00	0
ATOM	819	N	PHE	89	0.061	47.108	115.309	1.00	2.00	0
ATOM	821	CA	PHE	89	1.114	48.117	115.393	1.00	2.00	0
ATOM	822	CB	PHE	89	1.567	48.599	114.004	1.00	2.00	0
ATOM	823	CG	PHE	89	2.305	47.563	113.221	1.00	2.00	0
ATOM	824	CD1	PHE	89	1.617	46.543	112.578	1.00	2.00	0
ATOM	825	CD2	PHE	89	3.683	47.581	113.159	1.00	2.00	0
ATOM	826	CE1	PHE	89	2.284	45.547	111.885	1.00	2.00	0
ATOM	827	CE2	PHE	89	4.379	46.586	112.464	1.00	2.00	0

ATOM	828	CZ	PHE	89	3.673	45.565	111.826	1.00	2.00	0
ATOM	829	C	PHE	89	0.495	49.250	116.197	1.00	2.00	0
ATOM	830	O	PHE	89	-0.664	49.615	115.985	1.00	2.00	0
ATOM	831	N	LEU	90	1.271	49.797	117.124	1.00	4.99	0
ATOM	833	CA	LEU	90	0.810	50.856	118.014	1.00	4.99	0
ATOM	834	CB	LEU	90	1.519	50.702	119.370	1.00	2.00	0
ATOM	835	CG	LEU	90	1.516	49.291	119.991	1.00	2.00	0
ATOM	836	CD1	LEU	90	2.488	49.246	121.147	1.00	2.00	0
ATOM	837	CD2	LEU	90	0.111	48.870	120.402	1.00	2.00	0
ATOM	838	C	LEU	90	1.000	52.275	117.463	1.00	4.99	0
ATOM	839	O	LEU	90	1.382	53.196	118.200	1.00	2.00	0
ATOM	840	N	GLY	91	0.734	52.459	116.175	1.00	14.03	0
ATOM	842	CA	GLY	91	0.884	53.774	115.588	1.00	14.03	0
ATOM	843	C	GLY	91	2.307	54.139	115.209	1.00	14.03	0
ATOM	844	O	GLY	91	3.220	53.312	115.267	1.00	32.27	0
ATOM	845	N	ASP	92	2.471	55.400	114.820	1.00	2.00	0
ATOM	847	CA	ASP	92	3.736	55.978	114.382	1.00	2.00	0
ATOM	848	CB	ASP	92	4.670	56.170	115.576	1.00	2.00	0
ATOM	849	CG	ASP	92	4.185	57.239	116.525	1.00	2.00	0
ATOM	850	OD1	ASP	92	3.449	58.145	116.063	1.00	2.00	0
ATOM	851	OD2	ASP	92	4.541	57.177	117.725	1.00	2.00	0
ATOM	852	C	ASP	92	4.427	55.205	113.259	1.00	2.00	0
ATOM	853	O	ASP	92	5.515	54.631	113.422	1.00	2.00	0
ATOM	854	N	TYR	93	3.792	55.234	112.096	1.00	2.00	0
ATOM	856	CA	TYR	93	4.301	54.523	110.938	1.00	2.00	0
ATOM	857	CB	TYR	93	3.149	53.907	110.171	1.00	2.00	0
ATOM	858	CG	TYR	93	2.122	53.226	111.029	1.00	2.00	0
ATOM	859	CD1	TYR	93	0.875	53.801	111.227	1.00	2.00	0
ATOM	860	CE1	TYR	93	-0.086	53.176	112.004	1.00	2.00	0
ATOM	861	CD2	TYR	93	2.390	52.002	111.628	1.00	2.00	0
ATOM	862	CE2	TYR	93	1.445	51.362	112.405	1.00	2.00	0
ATOM	863	CZ	TYR	93	0.204	51.951	112.593	1.00	2.00	0
ATOM	864	OH	TYR	93	-0.736	51.315	113.379	1.00	2.00	0
ATOM	866	C	TYR	93	5.088	55.399	109.992	1.00	2.00	0
ATOM	867	O	TYR	93	5.998	54.922	109.335	1.00	2.00	0
ATOM	868	N	VAL	94	4.718	56.667	109.904	1.00	2.00	0
ATOM	870	CA	VAL	94	5.380	57.607	109.004	1.00	2.00	0
ATOM	871	CB	VAL	94	4.322	58.340	108.112	1.00	2.00	0
ATOM	872	CG1	VAL	94	3.365	57.315	107.523	1.00	2.00	0
ATOM	873	CG2	VAL	94	3.551	59.396	108.903	1.00	2.00	0
ATOM	874	C	VAL	94	6.253	58.614	109.780	1.00	2.00	0
ATOM	875	O	VAL	94	6.447	58.457	110.985	1.00	2.00	0
ATOM	876	N	ASP	95	6.774	59.629	109.094	1.00	8.40	0
ATOM	878	CA	ASP	95	7.641	60.648	109.689	1.00	2.00	0
ATOM	879	CB	ASP	95	6.967	61.356	110.868	1.00	39.32	0
ATOM	880	CG	ASP	95	5.975	62.433	110.449	1.00	45.35	0
ATOM	881	OD1	ASP	95	6.227	63.167	109.471	1.00	44.75	0
ATOM	882	OD2	ASP	95	4.937	62.561	111.127	1.00	53.79	0
ATOM	883	C	ASP	95	8.975	60.074	110.155	1.00	2.71	0
ATOM	884	O	ASP	95	9.092	58.877	110.421	1.00	37.69	0
ATOM	885	N	ARG	96	9.972	60.949	110.252	1.00	21.97	0
ATOM	887	CA	ARG	96	11.322	60.589	110.685	1.00	27.39	0
ATOM	888	CB	ARG	96	11.285	59.989	112.099	1.00	18.63	0
ATOM	889	CG	ARG	96	12.037	60.816	113.128	1.00	24.81	0
ATOM	890	CD	ARG	96	11.255	62.052	113.581	1.00	32.64	0
ATOM	891	NE	ARG	96	10.551	61.833	114.850	1.00	39.46	0
ATOM	893	CZ	ARG	96	9.890	62.774	115.525	1.00	39.86	0
ATOM	894	NH1	ARG	96	9.824	64.018	115.066	1.00	40.95	0
ATOM	897	NH2	ARG	96	9.290	62.471	116.670	1.00	44.56	0
ATOM	900	C	ARG	96	12.109	59.659	109.732	1.00	24.24	0
ATOM	901	O	ARG	96	13.114	60.072	109.135	1.00	13.09	0
ATOM	902	N	GLY	97	11.668	58.411	109.592	1.00	19.94	0
ATOM	904	CA	GLY	97	12.359	57.480	108.716	1.00	20.45	0
ATOM	905	C	GLY	97	12.412	57.920	107.269	1.00	23.76	0
ATOM	906	O	GLY	97	11.516	58.617	106.773	1.00	84.64	0
ATOM	907	N	LYS	98	13.460	57.469	106.584	1.00	47.57	0
ATOM	909	CA	LYS	98	13.698	57.806	105.182	1.00	46.79	0
ATOM	910	CB	LYS	98	15.147	57.462	104.832	1.00	31.45	0

ATOM	911	CG	LYS	98	16.169	58.397	105.487	1.00	30.73	0
ATOM	912	CD	LYS	98	17.606	58.061	105.087	1.00	32.79	0
ATOM	913	CE	LYS	98	18.605	59.089	105.627	1.00	30.08	0
ATOM	914	NZ	LYS	98	20.036	58.743	105.315	1.00	31.54	0
ATOM	918	C	LYS	98	12.741	57.196	104.146	1.00	44.78	0
ATOM	919	O	LYS	98	12.613	57.707	103.040	1.00	31.43	0
ATOM	920	N	GLN	99	12.059	56.120	104.517	1.00	2.00	0
ATOM	922	CA	GLN	99	11.132	55.430	103.639	1.00	2.00	0
ATOM	923	CB	GLN	99	11.654	54.023	103.337	1.00	11.21	0
ATOM	924	CG	GLN	99	12.945	53.993	102.552	1.00	6.66	0
ATOM	925	CD	GLN	99	13.361	52.586	102.177	1.00	11.01	0
ATOM	926	OE1	GLN	99	13.802	51.805	103.031	1.00	10.44	0
ATOM	927	NE2	GLN	99	13.229	52.247	100.895	1.00	8.18	0
ATOM	930	C	GLN	99	9.741	55.328	104.245	1.00	2.00	0
ATOM	931	O	GLN	99	9.177	54.238	104.317	1.00	6.66	0
ATOM	932	N	SER	100	9.178	56.460	104.657	1.00	24.01	0
ATOM	934	CA	SER	100	7.839	56.475	105.257	1.00	24.01	0
ATOM	935	CB	SER	100	7.481	57.897	105.739	1.00	2.00	0
ATOM	936	OG	SER	100	8.479	58.490	106.556	1.00	2.00	0
ATOM	938	C	SER	100	6.749	55.987	104.272	1.00	24.01	0
ATOM	939	O	SER	100	5.703	55.463	104.680	1.00	2.00	0
ATOM	940	N	LEU	101	7.015	56.153	102.977	1.00	27.83	0
ATOM	942	CA	LEU	101	6.084	55.786	101.913	1.00	27.83	0
ATOM	943	CB	LEU	101	6.551	56.416	100.599	1.00	3.66	0
ATOM	944	CG	LEU	101	5.593	57.224	99.721	1.00	3.66	0
ATOM	945	CD1	LEU	101	4.209	56.591	99.749	1.00	3.66	0
ATOM	946	CD2	LEU	101	5.532	58.653	100.208	1.00	3.66	0
ATOM	947	C	LEU	101	5.852	54.284	101.689	1.00	27.83	0
ATOM	948	O	LEU	101	4.731	53.851	101.467	1.00	3.66	0
ATOM	949	N	GLU	102	6.901	53.480	101.725	1.00	2.00	0
ATOM	951	CA	GLU	102	6.713	52.055	101.490	1.00	2.00	0
ATOM	952	CB	GLU	102	7.976	51.470	100.870	1.00	13.98	0
ATOM	953	CG	GLU	102	9.211	52.208	101.294	1.00	13.98	0
ATOM	954	CD	GLU	102	10.116	52.539	100.136	1.00	13.98	0
ATOM	955	OE1	GLU	102	10.181	53.727	99.737	1.00	13.98	0
ATOM	956	OE2	GLU	102	10.772	51.599	99.643	1.00	13.98	0
ATOM	957	C	GLU	102	6.307	51.324	102.763	1.00	2.00	0
ATOM	958	O	GLU	102	5.686	50.263	102.729	1.00	13.98	0
ATOM	959	N	THR	103	6.664	51.901	103.897	1.00	2.00	0
ATOM	961	CA	THR	103	6.293	51.330	105.173	1.00	2.00	0
ATOM	962	CB	THR	103	6.923	52.098	106.309	1.00	2.00	0
ATOM	963	OG1	THR	103	8.313	52.297	106.028	1.00	2.00	0
ATOM	965	CG2	THR	103	6.758	51.329	107.599	1.00	2.00	0
ATOM	966	C	THR	103	4.775	51.440	105.296	1.00	2.00	0
ATOM	967	O	THR	103	4.081	50.428	105.394	1.00	2.00	0
ATOM	968	N	ILE	104	4.256	52.667	105.257	1.00	2.00	0
ATOM	970	CA	ILE	104	2.824	52.873	105.363	1.00	2.00	0
ATOM	971	CB	ILE	104	2.486	54.389	105.300	1.00	12.72	0
ATOM	972	CG2	ILE	104	2.856	54.965	103.956	1.00	12.35	0
ATOM	973	CG1	ILE	104	0.996	54.618	105.548	1.00	13.84	0
ATOM	974	CD1	ILE	104	0.459	53.940	106.787	1.00	12.35	0
ATOM	975	C	ILE	104	2.074	52.062	104.294	1.00	2.00	0
ATOM	976	O	ILE	104	0.975	51.581	104.544	1.00	18.28	0
ATOM	977	N	CYS	105	2.690	51.868	103.127	1.00	23.45	0
ATOM	979	CA	CYS	105	2.080	51.092	102.042	1.00	21.74	0
ATOM	980	CB	CYS	105	2.722	51.458	100.708	1.00	20.76	0
ATOM	981	SG	CYS	105	2.010	52.958	99.957	1.00	18.03	0
ATOM	982	C	CYS	105	2.061	49.563	102.214	1.00	17.08	0
ATOM	983	O	CYS	105	1.114	48.915	101.781	1.00	20.76	0
ATOM	984	N	LEU	106	3.089	48.982	102.833	1.00	2.00	0
ATOM	986	CA	LEU	106	3.124	47.526	103.073	1.00	2.00	0
ATOM	987	CB	LEU	106	4.519	47.042	103.495	1.00	2.00	0
ATOM	988	CG	LEU	106	4.680	45.544	103.802	1.00	2.00	0
ATOM	989	CD1	LEU	106	4.200	44.694	102.639	1.00	2.00	0
ATOM	990	CD2	LEU	106	6.133	45.247	104.053	1.00	2.00	0
ATOM	991	C	LEU	106	2.154	47.179	104.178	1.00	2.00	0
ATOM	992	O	LEU	106	1.589	46.088	104.192	1.00	2.00	0
ATOM	993	N	LEU	107	1.992	48.107	105.116	1.00	2.00	0

ATOM	995	CA	LEU	107	1.078	47.922	106.226	1.00	2.00	0
ATOM	996	CB	LEU	107	1.347	48.967	107.319	1.00	2.00	0
ATOM	997	CG	LEU	107	2.761	48.857	107.911	1.00	2.00	0
ATOM	998	CD1	LEU	107	3.106	50.016	108.815	1.00	2.00	0
ATOM	999	CD2	LEU	107	2.868	47.535	108.638	1.00	2.00	0
ATOM	1000	C	LEU	107	-0.339	48.035	105.683	1.00	2.00	0
ATOM	1001	O	LEU	107	-1.153	47.125	105.873	1.00	2.00	0
ATOM	1002	N	LEU	108	-0.623	49.126	104.971	1.00	2.00	0
ATOM	1004	CA	LEU	108	-1.953	49.340	104.394	1.00	2.00	0
ATOM	1005	CB	LEU	108	-2.020	50.666	103.637	1.00	2.00	0
ATOM	1006	CG	LEU	108	-2.103	51.925	104.499	1.00	2.00	0
ATOM	1007	CD1	LEU	108	-2.244	53.164	103.618	1.00	2.00	0
ATOM	1008	CD2	LEU	108	-3.281	51.792	105.433	1.00	2.00	0
ATOM	1009	C	LEU	108	-2.352	48.206	103.455	1.00	2.00	0
ATOM	1010	O	LEU	108	-3.533	47.846	103.369	1.00	2.00	0
ATOM	1011	N	ALA	109	-1.366	47.643	102.762	1.00	2.00	0
ATOM	1013	CA	ALA	109	-1.608	46.539	101.839	1.00	2.00	0
ATOM	1014	CB	ALA	109	-0.336	46.209	101.087	1.00	33.06	0
ATOM	1015	C	ALA	109	-2.091	45.316	102.605	1.00	2.00	0
ATOM	1016	O	ALA	109	-3.146	44.746	102.305	1.00	24.92	0
ATOM	1017	N	TYR	110	-1.311	44.929	103.609	1.00	5.11	0
ATOM	1019	CA	TYR	110	-1.625	43.781	104.452	1.00	2.00	0
ATOM	1020	CB	TYR	110	-0.495	43.564	105.438	1.00	2.00	0
ATOM	1021	CG	TYR	110	0.674	42.771	104.922	1.00	2.00	0
ATOM	1022	CD1	TYR	110	1.966	43.235	105.092	1.00	2.00	0
ATOM	1023	CE1	TYR	110	3.053	42.474	104.706	1.00	2.00	0
ATOM	1024	CD2	TYR	110	0.494	41.517	104.340	1.00	2.00	0
ATOM	1025	CE2	TYR	110	1.578	40.743	103.950	1.00	2.00	0
ATOM	1026	CZ	TYR	110	2.859	41.230	104.139	1.00	2.00	0
ATOM	1027	OH	TYR	110	3.963	40.483	103.779	1.00	2.00	0
ATOM	1029	C	TYR	110	-2.948	43.940	105.215	1.00	2.00	0
ATOM	1030	O	TYR	110	-3.663	42.961	105.441	1.00	2.00	0
ATOM	1031	N	LYS	111	-3.265	45.168	105.618	1.00	2.00	0
ATOM	1033	CA	LYS	111	-4.508	45.430	106.333	1.00	2.00	0
ATOM	1034	CB	LYS	111	-4.619	46.904	106.708	1.00	2.00	0
ATOM	1035	CG	LYS	111	-5.942	47.262	107.393	1.00	2.00	0
ATOM	1036	CD	LYS	111	-6.085	46.501	108.685	1.00	2.00	0
ATOM	1037	CE	LYS	111	-7.410	46.743	109.354	1.00	2.00	0
ATOM	1038	NZ	LYS	111	-7.643	45.735	110.428	1.00	2.00	0
ATOM	1042	C	LYS	111	-5.698	45.051	105.465	1.00	2.00	0
ATOM	1043	O	LYS	111	-6.655	44.431	105.951	1.00	2.00	0
ATOM	1044	N	ILE	112	-5.624	45.455	104.192	1.00	2.00	0
ATOM	1046	CA	ILE	112	-6.651	45.192	103.177	1.00	2.00	0
ATOM	1047	CB	ILE	112	-6.361	45.978	101.875	1.00	25.04	0
ATOM	1048	CG2	ILE	112	-7.414	45.656	100.814	1.00	25.04	0
ATOM	1049	CG1	ILE	112	-6.339	47.482	102.166	1.00	25.04	0
ATOM	1050	CD1	ILE	112	-5.857	48.336	101.012	1.00	25.04	0
ATOM	1051	C	ILE	112	-6.706	43.706	102.829	1.00	2.00	0
ATOM	1052	O	ILE	112	-7.783	43.156	102.568	1.00	25.04	0
ATOM	1053	N	LYS	113	-5.537	43.067	102.816	1.00	2.00	0
ATOM	1055	CA	LYS	113	-5.447	41.649	102.513	1.00	2.00	0
ATOM	1056	CB	LYS	113	-4.001	41.285	102.181	1.00	8.72	0
ATOM	1057	CG	LYS	113	-3.852	39.909	101.596	1.00	8.72	0
ATOM	1058	CD	LYS	113	-2.780	39.871	100.521	1.00	8.72	0
ATOM	1059	CE	LYS	113	-2.618	38.467	99.975	1.00	8.72	0
ATOM	1060	NZ	LYS	113	-3.952	37.873	99.637	1.00	8.72	0
ATOM	1064	C	LYS	113	-5.987	40.780	103.667	1.00	2.00	0
ATOM	1065	O	LYS	113	-6.620	39.742	103.435	1.00	8.72	0
ATOM	1066	N	TYR	114	-5.744	41.200	104.906	1.00	9.02	0
ATOM	1068	CA	TYR	114	-6.226	40.455	106.068	1.00	8.11	0
ATOM	1069	CB	TYR	114	-5.122	39.580	106.666	1.00	12.47	0
ATOM	1070	CG	TYR	114	-4.138	38.988	105.689	1.00	12.47	0
ATOM	1071	CD1	TYR	114	-3.027	39.715	105.278	1.00	12.47	0
ATOM	1072	CE1	TYR	114	-2.111	39.191	104.397	1.00	12.47	0
ATOM	1073	CD2	TYR	114	-4.307	37.709	105.188	1.00	12.47	0
ATOM	1074	CE2	TYR	114	-3.395	37.168	104.302	1.00	12.47	0
ATOM	1075	CZ	TYR	114	-2.296	37.917	103.908	1.00	12.47	0
ATOM	1076	OH	TYR	114	-1.378	37.404	103.013	1.00	12.47	0

ATOM	1078	C	TYR	114	-6.729	41.417	107.155	1.00	9.78	0
ATOM	1079	O	TYR	114	-6.058	41.638	108.169	1.00	12.47	0
ATOM	1080	N	PRO	115	-7.928	41.985	106.968	1.00	34.30	0
ATOM	1081	CD	PRO	115	-8.843	41.845	105.826	1.00	24.86	0
ATOM	1082	CA	PRO	115	-8.488	42.912	107.944	1.00	34.30	0
ATOM	1083	CB	PRO	115	-9.862	43.227	107.365	1.00	24.86	0
ATOM	1084	CG	PRO	115	-9.640	43.117	105.921	1.00	24.86	0
ATOM	1085	C	PRO	115	-8.586	42.310	109.335	1.00	34.30	0
ATOM	1086	O	PRO	115	-8.017	42.837	110.285	1.00	24.86	0
ATOM	1087	N	GLU	116	-9.275	41.181	109.445	1.00	2.00	0
ATOM	1089	CA	GLU	116	-9.477	40.538	110.742	1.00	2.00	0
ATOM	1090	CB	GLU	116	-10.577	39.469	110.637	1.00	35.30	0
ATOM	1091	CG	GLU	116	-11.673	39.726	109.593	1.00	37.08	0
ATOM	1092	CD	GLU	116	-12.739	40.728	110.027	1.00	43.38	0
ATOM	1093	OE1	GLU	116	-13.060	41.641	109.235	1.00	47.93	0
ATOM	1094	OE2	GLU	116	-13.274	40.599	111.147	1.00	48.80	0
ATOM	1095	C	GLU	116	-8.213	39.902	111.358	1.00	2.00	0
ATOM	1096	O	GLU	116	-8.296	39.287	112.424	1.00	32.95	0
ATOM	1097	N	ASN	117	-7.054	40.067	110.712	1.00	2.00	0
ATOM	1099	CA	ASN	117	-5.820	39.455	111.211	1.00	2.00	0
ATOM	1100	CB	ASN	117	-5.457	38.220	110.375	1.00	6.12	0
ATOM	1101	CG	ASN	117	-6.552	37.174	110.353	1.00	8.10	0
ATOM	1102	OD1	ASN	117	-7.584	37.351	109.700	1.00	17.57	0
ATOM	1103	ND2	ASN	117	-6.328	36.071	111.048	1.00	14.33	0
ATOM	1106	C	ASN	117	-4.613	40.372	111.211	1.00	2.00	0
ATOM	1107	O	ASN	117	-3.496	39.952	111.506	1.00	8.94	0
ATOM	1108	N	PHE	118	-4.821	41.620	110.862	1.00	2.00	0
ATOM	1110	CA	PHE	118	-3.715	42.559	110.815	1.00	2.00	0
ATOM	1111	CB	PHE	118	-3.135	42.617	109.395	1.00	2.00	0
ATOM	1112	CG	PHE	118	-1.902	43.471	109.256	1.00	2.00	0
ATOM	1113	CD1	PHE	118	-0.647	42.886	109.155	1.00	2.00	0
ATOM	1114	CD2	PHE	118	-1.995	44.857	109.177	1.00	2.00	0
ATOM	1115	CE1	PHE	118	0.503	43.680	108.972	1.00	2.00	0
ATOM	1116	CE2	PHE	118	-0.857	45.647	108.997	1.00	2.00	0
ATOM	1117	CZ	PHE	118	0.393	45.060	108.894	1.00	2.00	0
ATOM	1118	C	PHE	118	-4.392	43.854	111.194	1.00	2.00	0
ATOM	1119	O	PHE	118	-5.384	44.259	110.576	1.00	2.00	0
ATOM	1120	N	PHE	119	-3.874	44.483	112.240	1.00	12.11	0
ATOM	1122	CA	PHE	119	-4.467	45.700	112.721	1.00	12.11	0
ATOM	1123	CB	PHE	119	-5.174	45.400	114.022	1.00	2.00	0
ATOM	1124	CG	PHE	119	-6.229	44.355	113.889	1.00	2.00	0
ATOM	1125	CD1	PHE	119	-5.903	43.008	113.975	1.00	2.00	0
ATOM	1126	CD2	PHE	119	-7.556	44.716	113.655	1.00	2.00	0
ATOM	1127	CE1	PHE	119	-6.881	42.035	113.829	1.00	2.00	0
ATOM	1128	CE2	PHE	119	-8.546	43.753	113.506	1.00	2.00	0
ATOM	1129	CZ	PHE	119	-8.209	42.410	113.592	1.00	2.00	0
ATOM	1130	C	PHE	119	-3.472	46.806	112.905	1.00	12.11	0
ATOM	1131	O	PHE	119	-2.342	46.577	113.346	1.00	2.00	0
ATOM	1132	N	LEU	120	-3.893	48.008	112.537	1.00	2.00	0
ATOM	1134	CA	LEU	120	-3.043	49.179	112.672	1.00	2.00	0
ATOM	1135	CB	LEU	120	-2.770	49.809	111.303	1.00	2.00	0
ATOM	1136	CG	LEU	120	-2.127	48.910	110.259	1.00	2.00	0
ATOM	1137	CD1	LEU	120	-2.147	49.623	108.924	1.00	2.00	0
ATOM	1138	CD2	LEU	120	-0.731	48.539	110.685	1.00	2.00	0
ATOM	1139	C	LEU	120	-3.766	50.176	113.559	1.00	2.00	0
ATOM	1140	O	LEU	120	-4.963	50.401	113.375	1.00	2.00	0
ATOM	1141	N	LEU	121	-3.069	50.730	114.542	1.00	2.00	0
ATOM	1143	CA	LEU	121	-3.670	51.714	115.415	1.00	2.00	0
ATOM	1144	CB	LEU	121	-3.351	51.428	116.890	1.00	2.00	0
ATOM	1145	CG	LEU	121	-4.142	50.320	117.598	1.00	2.00	0
ATOM	1146	CD1	LEU	121	-3.648	50.150	119.012	1.00	2.00	0
ATOM	1147	CD2	LEU	121	-5.609	50.657	117.581	1.00	2.00	0
ATOM	1148	C	LEU	121	-3.106	53.060	115.004	1.00	2.00	0
ATOM	1149	O	LEU	121	-2.213	53.148	114.166	1.00	2.00	0
ATOM	1150	N	ARG	122	-3.631	54.118	115.592	1.00	2.00	0
ATOM	1152	CA	ARG	122	-3.162	55.434	115.251	1.00	2.00	0
ATOM	1153	CB	ARG	122	-4.336	56.404	115.224	1.00	2.00	0
ATOM	1154	CG	ARG	122	-4.047	57.765	114.619	1.00	2.00	0

ATOM	1155	CD	ARG	122	-5.298	58.565	114.683	1.00	2.00	0
ATOM	1156	NE	ARG	122	-5.207	59.851	114.014	1.00	2.00	0
ATOM	1158	CZ	ARG	122	-6.274	60.578	113.685	1.00	2.00	0
ATOM	1159	NH1	ARG	122	-7.512	60.131	113.956	1.00	2.00	0
ATOM	1162	NH2	ARG	122	-6.104	61.762	113.102	1.00	2.00	0
ATOM	1165	C	ARG	122	-2.104	55.942	116.208	1.00	2.00	0
ATOM	1166	O	ARG	122	-2.163	55.716	117.423	1.00	2.00	0
ATOM	1167	N	GLY	123	-1.135	56.635	115.631	1.00	2.00	0
ATOM	1169	CA	GLY	123	-0.073	57.235	116.399	1.00	2.00	0
ATOM	1170	C	GLY	123	-0.205	58.730	116.198	1.00	2.00	0
ATOM	1171	O	GLY	123	-0.865	59.177	115.262	1.00	86.19	0
ATOM	1172	N	ASN	124	0.437	59.508	117.058	1.00	2.00	0
ATOM	1174	CA	ASN	124	0.390	60.956	116.958	1.00	2.00	0
ATOM	1175	CB	ASN	124	1.003	61.584	118.199	1.00	4.11	0
ATOM	1176	CG	ASN	124	2.477	61.333	118.313	1.00	8.88	0
ATOM	1177	OD1	ASN	124	2.940	60.187	118.486	1.00	8.54	0
ATOM	1178	ND2	ASN	124	3.240	62.400	118.236	1.00	6.38	0
ATOM	1181	C	ASN	124	1.103	61.455	115.708	1.00	2.00	0
ATOM	1182	O	ASN	124	1.143	62.664	115.430	1.00	5.53	0
ATOM	1183	N	HIS	125	1.678	60.515	114.963	1.00	18.81	0
ATOM	1185	CA	HIS	125	2.372	60.815	113.723	1.00	19.06	0
ATOM	1186	CB	HIS	125	3.759	60.186	113.744	1.00	13.41	0
ATOM	1187	CG	HIS	125	4.790	61.072	114.362	1.00	13.65	0
ATOM	1188	CD2	HIS	125	4.765	61.811	115.493	1.00	8.85	0
ATOM	1189	ND1	HIS	125	6.006	61.322	113.772	1.00	14.49	0
ATOM	1191	CE1	HIS	125	6.686	62.182	114.503	1.00	13.93	0
ATOM	1192	NE2	HIS	125	5.954	62.496	115.554	1.00	12.46	0
ATOM	1194	C	HIS	125	1.555	60.338	112.523	1.00	16.39	0
ATOM	1195	O	HIS	125	2.090	59.905	111.513	1.00	13.34	0
ATOM	1196	N	GLU	126	0.241	60.382	112.686	1.00	2.00	0
ATOM	1198	CA	GLU	126	-0.731	60.018	111.664	1.00	2.00	0
ATOM	1199	CB	GLU	126	-1.462	58.725	112.050	1.00	2.00	0
ATOM	1200	CG	GLU	126	-0.783	57.443	111.570	1.00	2.00	0
ATOM	1201	CD	GLU	126	0.578	57.217	112.190	1.00	2.00	0
ATOM	1202	OE1	GLU	126	1.615	57.346	111.504	1.00	2.00	0
ATOM	1203	OE2	GLU	126	0.610	56.898	113.385	1.00	2.00	0
ATOM	1204	C	GLU	126	-1.683	61.211	111.705	1.00	2.00	0
ATOM	1205	O	GLU	126	-2.903	61.073	111.837	1.00	2.00	0
ATOM	1206	N	CYS	127	-1.097	62.392	111.578	1.00	2.00	0
ATOM	1208	CA	CYS	127	-1.860	63.608	111.681	1.00	2.00	0
ATOM	1209	CB	CYS	127	-2.037	63.960	113.167	1.00	26.08	0
ATOM	1210	SG	CYS	127	-3.052	65.420	113.546	1.00	39.49	0
ATOM	1211	C	CYS	127	-1.142	64.731	110.976	1.00	2.00	0
ATOM	1212	O	CYS	127	0.048	64.974	111.204	1.00	23.46	0
ATOM	1213	N	ALA	128	-1.912	65.421	110.142	1.00	2.00	0
ATOM	1215	CA	ALA	128	-1:489	66.551	109.335	1.00	2.00	0
ATOM	1216	CB	ALA	128	-2.686	67.412	109.031	1.00	2.00	0
ATOM	1217	C	ALA	128	-0.385	67.413	109.910	1.00	2.00	0
ATOM	1218	O	ALA	128	0.690	67.456	109.346	1.00	2.00	0
ATOM	1219	N	SER	129	-0.649	68.097	111.021	1.00	2.00	0
ATOM	1221	CA	SER	129	0.331	68.981	111.675	1.00	2.00	0
ATOM	1222	CB	SER	129	-0.288	69.580	112.937	1.00	28.29	0
ATOM	1223	OG	SER	129	-0.836	68.562	113.760	1.00	32.64	0
ATOM	1225	C	SER	129	1.671	68.344	112.042	1.00	2.00	0
ATOM	1226	O	SER	129	2.669	69.048	112.186	1.00	24.43	0
ATOM	1227	N	ILE	130	1.687	67.027	112.226	1.00	2.00	0
ATOM	1229	CA	ILE	130	2.920	66.343	112.572	1.00	2.00	0
ATOM	1230	CB	ILE	130	2.671	65.177	113.588	1.00	2.00	0
ATOM	1231	CG2	ILE	130	3.999	64.584	114.058	1.00	2.00	0
ATOM	1232	CG1	ILE	130	2.012	65.717	114.854	1.00	2.00	0
ATOM	1233	CD1	ILE	130	2.828	66.820	115.554	1.00	2.00	0
ATOM	1234	C	ILE	130	3.563	65.829	111.289	1.00	2.00	0
ATOM	1235	O	ILE	130	4.776	65.962	111.113	1.00	2.00	0
ATOM	1236	N	ASN	131	2.751	65.253	110.397	1.00	15.50	0
ATOM	1238	CA	ASN	131	3.209	64.747	109.091	1.00	12.35	0
ATOM	1239	CB	ASN	131	2.027	64.290	108.231	1.00	2.00	0
ATOM	1240	CG	ASN	131	1.487	62.929	108.632	1.00	2.00	0
ATOM	1241	OD1	ASN	131	1.712	62.438	109.750	1.00	2.00	0

ATOM	1242	ND2	ASN	131	0.745	62.313	107.718	1.00	2.00	0
ATOM	1245	C	ASN	131	3.849	65.914	108.374	1.00	28.24	0
ATOM	1246	O	ASN	131	5.001	65.854	107.951	1.00	2.00	0
ATOM	1247	N	ARG	132	3.051	66.971	108.255	1.00	2.00	0
ATOM	1249	CA	ARG	132	3.386	68.234	107.627	1.00	2.00	0
ATOM	1250	CB	ARG	132	2.327	69.269	108.006	1.00	22.25	0
ATOM	1251	CG	ARG	132	2.505	70.673	107.477	1.00	26.48	0
ATOM	1252	CD	ARG	132	2.505	70.734	105.962	1.00	27.28	0
ATOM	1253	NE	ARG	132	3.849	70.533	105.434	1.00	36.02	0
ATOM	1255	CZ	ARG	132	4.577	71.479	104.852	1.00	34.03	0
ATOM	1256	NH1	ARG	132	4.080	72.697	104.711	1.00	30.29	0
ATOM	1259	NH2	ARG	132	5.808	71.211	104.424	1.00	37.77	0
ATOM	1262	C	ARG	132	4.768	68.731	107.990	1.00	2.00	0
ATOM	1263	O	ARG	132	5.359	69.477	107.225	1.00	27.60	0
ATOM	1264	N	ILE	133	5.314	68.324	109.127	1.00	2.00	0
ATOM	1266	CA	ILE	133	6.652	68.801	109.457	1.00	2.00	0
ATOM	1267	CB	ILE	133	6.652	69.644	110.746	1.00	20.12	0
ATOM	1268	CG2	ILE	133	6.215	71.055	110.441	1.00	19.34	0
ATOM	1269	CG1	ILE	133	5.761	68.999	111.800	1.00	21.76	0
ATOM	1270	CD1	ILE	133	5.687	69.792	113.065	1.00	22.74	0
ATOM	1271	C	ILE	133	7.794	67.779	109.553	1.00	2.00	0
ATOM	1272	O	ILE	133	8.915	68.073	109.127	1.00	21.74	0
ATOM	1273	N	TYR	134	7.521	66.583	110.080	1.00	2.00	0
ATOM	1275	CA	TYR	134	8.571	65.567	110.270	1.00	2.00	0
ATOM	1276	CB	TYR	134	8.330	64.766	111.561	1.00	27.01	0
ATOM	1277	CG	TYR	134	8.270	65.648	112.767	1.00	19.94	0
ATOM	1278	CD1	TYR	134	7.092	65.789	113.486	1.00	23.86	0
ATOM	1279	CE1	TYR	134	7.016	66.651	114.557	1.00	24.86	0
ATOM	1280	CD2	TYR	134	9.380	66.392	113.160	1.00	24.55	0
ATOM	1281	CE2	TYR	134	9.312	67.254	114.228	1.00	23.33	0
ATOM	1282	CZ	TYR	134	8.128	67.384	114.925	1.00	28.93	0
ATOM	1283	OH	TYR	134	8.043	68.259	115.984	1.00	27.73	0
ATOM	1285	C	TYR	134	8.823	64.606	109.139	1.00	2.00	0
ATOM	1286	O	TYR	134	8.986	63.404	109.368	1.00	24.62	0
ATOM	1287	N	GLY	135	8.847	65.127	107.922	1.00	11.68	0
ATOM	1289	CA	GLY	135	9.134	64.275	106.787	1.00	10.40	0
ATOM	1290	C	GLY	135	8.028	63.772	105.882	1.00	9.03	0
ATOM	1291	O	GLY	135	8.010	64.127	104.713	1.00	20.70	0
ATOM	1292	N	PHE	136	7.110	62.963	106.393	1.00	2.00	0
ATOM	1294	CA	PHE	136	6.062	62.412	105.549	1.00	2.00	0
ATOM	1295	CB	PHE	136	4.951	61.757	106.347	1.00	2.00	0
ATOM	1296	CG	PHE	136	4.091	60.831	105.524	1.00	2.00	0
ATOM	1297	CD1	PHE	136	4.664	59.734	104.870	1.00	2.00	0
ATOM	1298	CD2	PHE	136	2.713	61.036	105.424	1.00	2.00	0
ATOM	1299	CE1	PHE	136	3.882	58.846	104.131	1.00	2.00	0
ATOM	1300	CE2	PHE	136	1.915	60.155	104.688	1.00	2.00	0
ATOM	1301	CZ	PHE	136	2.507	59.050	104.037	1.00	2.00	0
ATOM	1302	C	PHE	136	5.421	63.358	104.563	1.00	2.00	0
ATOM	1303	O	PHE	136	5.121	62.926	103.445	1.00	2.00	0
ATOM	1304	N	TYR	137	5.199	64.616	104.940	1.00	2.00	0
ATOM	1306	CA	TYR	137	4.606	65.530	103.977	1.00	2.00	0
ATOM	1307	CB	TYR	137	4.243	66.859	104.598	1.00	2.00	0
ATOM	1308	CG	TYR	137	3.886	67.921	103.564	1.00	2.00	0
ATOM	1309	CD1	TYR	137	2.550	68.203	103.257	1.00	2.00	0
ATOM	1310	CE1	TYR	137	2.228	69.196	102.327	1.00	2.00	0
ATOM	1311	CD2	TYR	137	4.893	68.666	102.901	1.00	2.00	0
ATOM	1312	CE2	TYR	137	4.576	69.644	101.985	1.00	2.00	0
ATOM	1313	CZ	TYR	137	3.247	69.903	101.707	1.00	2.00	0
ATOM	1314	OH	TYR	137	2.920	70.893	100.823	1.00	2.00	0
ATOM	1316	C	TYR	137	5.566	65.785	102.822	1.00	2.00	0
ATOM	1317	O	TYR	137	5.187	65.669	101.646	1.00	2.00	0
ATOM	1318	N	ASP	138	6.802	66.153	103.155	1.00	2.00	0
ATOM	1320	CA	ASP	138	7.822	66.439	102.147	1.00	2.00	0
ATOM	1321	CB	ASP	138	9.102	66.971	102.810	1.00	28.59	0
ATOM	1322	CG	ASP	138	8.832	68.173	103.705	1.00	31.85	0
ATOM	1323	OD1	ASP	138	8.999	69.327	103.255	1.00	34.04	0
ATOM	1324	OD2	ASP	138	8.432	67.963	104.867	1.00	31.26	0
ATOM	1325	C	ASP	138	8.118	65.203	101.308	1.00	2.00	0

ATOM	1326	O	ASP	138	8.322	65.309	100.102	1.00	27.39	0
ATOM	1327	N	GLU	139	8.097	64.030	101.926	1.00	31.40	0
ATOM	1329	CA	GLU	139	8.366	62.797	101.200	1.00	28.32	0
ATOM	1330	CB	GLU	139	8.380	61.608	102.149	1.00	2.00	0
ATOM	1331	CG	GLU	139	8.965	60.361	101.526	1.00	4.78	0
ATOM	1332	CD	GLU	139	9.167	59.231	102.525	1.00	3.01	0
ATOM	1333	OE1	GLU	139	9.135	58.050	102.087	1.00	2.00	0
ATOM	1334	OE2	GLU	139	9.372	59.518	103.738	1.00	4.61	0
ATOM	1335	C	GLU	139	7.323	62.572	100.117	1.00	30.47	0
ATOM	1336	O	GLU	139	7.660	62.419	98.941	1.00	2.00	0
ATOM	1337	N	CYS	140	6.055	62.553	100.511	1.00	12.32	0
ATOM	1339	CA	CYS	140	4.981	62.355	99.553	1.00	3.99	0
ATOM	1340	CB	CYS	140	3.625	62.543	100.221	1.00	18.56	0
ATOM	1341	SG	CYS	140	3.313	61.308	101.477	1.00	23.54	0
ATOM	1342	C	CYS	140	5.128	63.346	98.416	1.00	12.32	0
ATOM	1343	O	CYS	140	5.117	62.961	97.257	1.00	21.26	0
ATOM	1344	N	LYS	141	5.305	64.616	98.763	1.00	41.55	0
ATOM	1346	CA	LYS	141	5.446	65.696	97.786	1.00	40.86	0
ATOM	1347	CB	LYS	141	5.655	67.023	98.531	1.00	38.66	0
ATOM	1348	CG	LYS	141	5.853	68.246	97.646	1.00	32.19	0
ATOM	1349	CD	LYS	141	5.886	69.522	98.468	1.00	35.28	0
ATOM	1350	CE	LYS	141	5.895	70.750	97.584	1.00	36.09	0
ATOM	1351	NZ	LYS	141	5.552	71.948	98.380	1.00	40.44	0
ATOM	1355	C	LYS	141	6.586	65.467	96.791	1.00	40.27	0
ATOM	1356	O	LYS	141	6.431	65.642	95.582	1.00	28.60	0
ATOM	1357	N	ARG	142	7.731	65.073	97.319	1.00	23.84	0
ATOM	1359	CA	ARG	142	8.912	64.834	96.512	1.00	23.84	0
ATOM	1360	CB	ARG	142	10.097	64.566	97.444	1.00	22.75	0
ATOM	1361	CG	ARG	142	11.368	64.101	96.778	1.00	24.10	0
ATOM	1362	CD	ARG	142	12.474	64.073	97.799	1.00	33.58	0
ATOM	1363	NE	ARG	142	12.099	63.283	98.963	1.00	37.62	0
ATOM	1365	CZ	ARG	142	12.464	62.018	99.150	1.00	46.30	0
ATOM	1366	NH1	ARG	142	13.224	61.404	98.249	1.00	44.23	0
ATOM	1369	NH2	ARG	142	12.060	61.363	100.234	1.00	42.22	0
ATOM	1372	C	ARG	142	8.732	63.689	95.519	1.00	23.84	0
ATOM	1373	O	ARG	142	8.995	63.838	94.330	1.00	24.93	0
ATOM	1374	N	ARG	143	8.268	62.550	95.999	1.00	2.00	0
ATOM	1376	CA	ARG	143	8.104	61.413	95.125	1.00	2.00	0
ATOM	1377	CB	ARG	143	8.267	60.134	95.941	1.00	2.86	0
ATOM	1378	CG	ARG	143	9.686	59.941	96.455	1.00	2.86	0
ATOM	1379	CD	ARG	143	9.792	58.874	97.530	1.00	8.64	0
ATOM	1380	NE	ARG	143	9.490	57.527	97.049	1.00	4.03	0
ATOM	1382	CZ	ARG	143	9.492	56.439	97.816	1.00	6.91	0
ATOM	1383	NH1	ARG	143	9.782	56.527	99.115	1.00	7.13	0
ATOM	1386	NH2	ARG	143	9.203	55.257	97.287	1.00	12.97	0
ATOM	1389	C	ARG	143	6.796	61.411	94.367	1.00	2.00	0
ATOM	1390	O	ARG	143	6.707	60.818	93.295	1.00	12.04	0
ATOM	1391	N	TYR	144	5.791	62.097	94.897	1.00	2.00	0
ATOM	1393	CA	TYR	144	4.459	62.120	94.274	1.00	2.00	0
ATOM	1394	CB	TYR	144	3.509	61.150	95.021	1.00	2.00	0
ATOM	1395	CG	TYR	144	3.902	59.689	94.953	1.00	2.00	0
ATOM	1396	CD1	TYR	144	4.946	59.203	95.716	1.00	2.00	0
ATOM	1397	CE1	TYR	144	5.336	57.885	95.635	1.00	2.00	0
ATOM	1398	CD2	TYR	144	3.248	58.804	94.102	1.00	2.00	0
ATOM	1399	CE2	TYR	144	3.633	57.483	94.017	1.00	2.00	0
ATOM	1400	CZ	TYR	144	4.683	57.034	94.786	1.00	2.00	0
ATOM	1401	OH	TYR	144	5.113	55.738	94.703	1.00	2.00	0
ATOM	1403	C	TYR	144	3.789	63.502	94.169	1.00	2.00	0
ATOM	1404	O	TYR	144	4.129	64.316	93.297	1.00	2.00	0
ATOM	1405	N	ASN	145	2.827	63.750	95.058	1.00	2.00	0
ATOM	1407	CA	ASN	145	2.081	65.000	95.083	1.00	2.00	0
ATOM	1408	CB	ASN	145	1.159	65.078	93.867	1.00	7.57	0
ATOM	1409	CG	ASN	145	0.255	63.861	93.748	1.00	5.76	0
ATOM	1410	OD1	ASN	145	-0.823	63.826	94.329	1.00	9.42	0
ATOM	1411	ND2	ASN	145	0.702	62.851	93.007	1.00	5.88	0
ATOM	1414	C	ASN	145	1.229	65.137	96.354	1.00	2.00	0
ATOM	1415	O	ASN	145	0.760	64.143	96.938	1.00	11.61	0
ATOM	1416	N	ILE	146	1.001	66.391	96.737	1.00	2.00	0

ATOM	1418	CA	ILE	146	0.217	66.745	97.901	1.00	2.00	0
ATOM	1419	CB	ILE	146	0.168	68.278	98.048	1.00	2.00	0
ATOM	1420	CG2	ILE	146	-0.607	68.690	99.278	1.00	2.00	0
ATOM	1421	CG1	ILE	146	1.591	68.798	98.201	1.00	2.00	0
ATOM	1422	CD1	ILE	146	1.679	70.270	98.360	1.00	2.00	0
ATOM	1423	C	ILE	146	-1.181	66.143	97.851	1.00	2.00	0
ATOM	1424	O	ILE	146	-1.805	65.927	98.881	1.00	2.00	0
ATOM	1425	N	LYS	147	-1.680	65.839	96.668	1.00	2.00	0
ATOM	1427	CA	LYS	147	-3.000	65.241	96.594	1.00	2.00	0
ATOM	1428	CB	LYS	147	-3.412	65.007	95.131	1.00	15.32	0
ATOM	1429	CG	LYS	147	-4.880	64.643	94.902	1.00	21.64	0
ATOM	1430	CD	LYS	147	-5.024	63.248	94.280	1.00	29.48	0
ATOM	1431	CE	LYS	147	-4.704	62.128	95.300	1.00	25.79	0
ATOM	1432	NZ	LYS	147	-4.388	60.777	94.716	1.00	22.31	0
ATOM	1436	C	LYS	147	-2.864	63.928	97.345	1.00	2.00	0
ATOM	1437	O	LYS	147	-3.652	63.630	98.233	1.00	8.30	0
ATOM	1438	N	LEU	148	-1.815	63.180	97.023	1.00	9.36	0
ATOM	1440	CA	LEU	148	-1.582	61.892	97.651	1.00	9.36	0
ATOM	1441	CB	LEU	148	-0.360	61.202	97.037	1.00	2.00	0
ATOM	1442	CG	LEU	148	-0.207	59.721	97.415	1.00	2.00	0
ATOM	1443	CD1	LEU	148	-1.398	58.910	96.924	1.00	2.00	0
ATOM	1444	CD2	LEU	148	1.078	59.168	96.835	1.00	2.00	0
ATOM	1445	C	LEU	148	-1.423	62.040	99.157	1.00	9.36	0
ATOM	1446	O	LEU	148	-2.097	61.351	99.899	1.00	2.00	0
ATOM	1447	N	TRP	149	-0.555	62.943	99.611	1.00	2.00	0
ATOM	1449	CA	TRP	149	-0.360	63.166	101.042	1.00	2.00	0
ATOM	1450	CB	TRP	149	0.559	64.359	101.276	1.00	9.48	0
ATOM	1451	CG	TRP	149	0.690	64.767	102.748	1.00	13.35	0
ATOM	1452	CD2	TRP	149	0.095	65.915	103.387	1.00	9.36	0
ATOM	1453	CE2	TRP	149	0.512	65.907	104.725	1.00	12.67	0
ATOM	1454	CE3	TRP	149	-0.751	66.946	102.951	1.00	9.36	0
ATOM	1455	CD1	TRP	149	1.415	64.135	103.713	1.00	12.84	0
ATOM	1456	NE1	TRP	149	1.315	64.811	104.895	1.00	14.40	0
ATOM	1458	CZ2	TRP	149	0.119	66.880	105.632	1.00	10.82	0
ATOM	1459	CZ3	TRP	149	-1.138	67.912	103.858	1.00	10.25	0
ATOM	1460	CH2	TRP	149	-0.702	67.870	105.182	1.00	21.34	0
ATOM	1461	C	TRP	149	-1.712	63.427	101.707	1.00	2.00	0
ATOM	1462	O	TRP	149	-2.095	62.726	102.647	1.00	9.36	0
ATOM	1463	N	LYS	150	-2.429	64.434	101.216	1.00	2.00	0
ATOM	1465	CA	LYS	150	-3.756	64.777	101.725	1.00	2.00	0
ATOM	1466	CB	LYS	150	-4.392	65.810	100.819	1.00	25.82	0
ATOM	1467	CG	LYS	150	-3.695	67.135	100.844	1.00	27.78	0
ATOM	1468	CD	LYS	150	-4.145	67.981	99.676	1.00	24.78	0
ATOM	1469	CE	LYS	150	-4.236	69.442	100.053	1.00	28.33	0
ATOM	1470	NZ	LYS	150	-5.243	69.673	101.132	1.00	35.49	0
ATOM	1474	C	LYS	150	-4.661	63.536	101.786	1.00	2.00	0
ATOM	1475	O	LYS	150	-5.468	63.397	102.701	1.00	28.71	0
ATOM	1476	N	THR	151	-4.525	62.638	100.809	1.00	2.00	0
ATOM	1478	CA	THR	151	-5.315	61.403	100.758	1.00	2.00	0
ATOM	1479	CB	THR	151	-5.111	60.670	99.408	1.00	18.71	0
ATOM	1480	OG1	THR	151	-5.491	61.532	98.332	1.00	21.97	0
ATOM	1482	CG2	THR	151	-5.964	59.434	99.332	1.00	19.85	0
ATOM	1483	C	THR	151	-4.920	60.487	101.925	1.00	2.00	0
ATOM	1484	O	THR	151	-5.760	59.773	102.489	1.00	14.71	0
ATOM	1485	N	PHE	152	-3.645	60.529	102.297	1.00	2.00	0
ATOM	1487	CA	PHE	152	-3.161	59.729	103.398	1.00	2.00	0
ATOM	1488	CB	PHE	152	-1.638	59.759	103.502	1.00	13.78	0
ATOM	1489	CG	PHE	152	-0.956	58.586	102.830	1.00	13.78	0
ATOM	1490	CD1	PHE	152	0.034	58.792	101.864	1.00	13.78	0
ATOM	1491	CD2	PHE	152	-1.289	57.277	103.178	1.00	13.78	0
ATOM	1492	CE1	PHE	152	0.679	57.717	101.260	1.00	13.78	0
ATOM	1493	CE2	PHE	152	-0.648	56.194	102.578	1.00	13.78	0
ATOM	1494	CZ	PHE	152	0.340	56.417	101.617	1.00	13.78	0
ATOM	1495	C	PHE	152	-3.767	60.246	104.673	1.00	2.00	0
ATOM	1496	O	PHE	152	-4.380	59.470	105.397	1.00	13.78	0
ATOM	1497	N	THR	153	-3.657	61.547	104.944	1.00	2.00	0
ATOM	1499	CA	THR	153	-4.217	62.064	106.192	1.00	2.00	0
ATOM	1500	CB	THR	153	-4.166	63.604	106.318	1.00	19.49	0

ATOM	1501	OG1	THR	153	-4.912	64.207	105.265	1.00	24.34	0
ATOM	1503	CG2	THR	153	-2.739	64.095	106.293	1.00	23.93	0
ATOM	1504	C	THR	153	-5.653	61.607	106.348	1.00	2.00	0
ATOM	1505	O	THR	153	-6.054	61.158	107.414	1.00	29.22	0
ATOM	1506	N	ASP	154	-6.415	61.667	105.276	1.00	2.00	0
ATOM	1508	CA	ASP	154	-7.801	61.250	105.332	1.00	2.00	0
ATOM	1509	CB	ASP	154	-8.442	61.393	103.945	1.00	21.48	0
ATOM	1510	CG	ASP	154	-9.965	61.345	103.987	1.00	21.21	0
ATOM	1511	OD1	ASP	154	-10.576	61.750	102.971	1.00	27.37	0
ATOM	1512	OD2	ASP	154	-10.548	60.912	105.018	1.00	20.95	0
ATOM	1513	C	ASP	154	-7.889	59.806	105.801	1.00	2.00	0
ATOM	1514	O	ASP	154	-8.783	59.444	106.569	1.00	11.19	0
ATOM	1515	N	CYS	155	-6.968	58.981	105.319	1.00	2.00	0
ATOM	1517	CA	CYS	155	-6.951	57.571	105.691	1.00	2.00	0
ATOM	1518	CB	CYS	155	-5.904	56.822	104.865	1.00	2.00	0
ATOM	1519	SG	CYS	155	-5.770	55.072	105.254	1.00	2.00	0
ATOM	1520	C	CYS	155	-6.627	57.479	107.178	1.00	2.00	0
ATOM	1521	O	CYS	155	-7.267	56.741	107.931	1.00	2.00	0
ATOM	1522	N	PHE	156	-5.641	58.273	107.583	1.00	8.58	0
ATOM	1524	CA	PHE	156	-5.172	58.366	108.954	1.00	8.58	0
ATOM	1525	CB	PHE	156	-4.056	59.409	109.018	1.00	2.00	0
ATOM	1526	CG	PHE	156	-2.766	58.945	108.437	1.00	2.00	0
ATOM	1527	CD1	PHE	156	-2.537	57.585	108.206	1.00	2.00	0
ATOM	1528	CD2	PHE	156	-1.756	59.847	108.160	1.00	2.00	0
ATOM	1529	CE1	PHE	156	-1.309	57.130	107.710	1.00	2.00	0
ATOM	1530	CE2	PHE	156	-0.518	59.400	107.662	1.00	2.00	0
ATOM	1531	CZ	PHE	156	-0.295	58.039	107.439	1.00	2.00	0
ATOM	1532	C	PHE	156	-6.287	58.743	109.931	1.00	8.58	0
ATOM	1533	O	PHE	156	-6.463	58.119	110.974	1.00	2.00	0
ATOM	1534	N	ASN	157	-7.055	59.758	109.572	1.00	2.00	0
ATOM	1536	CA	ASN	157	-8.144	60.233	110.405	1.00	2.00	0
ATOM	1537	CB	ASN	157	-8.811	61.475	109.779	1.00	2.00	0
ATOM	1538	CG	ASN	157	-7.861	62.661	109.577	1.00	2.00	0
ATOM	1539	OD1	ASN	157	-8.226	63.629	108.922	1.00	2.00	0
ATOM	1540	ND2	ASN	157	-6.669	62.601	110.143	1.00	2.00	0
ATOM	1543	C	ASN	157	-9.230	59.179	110.631	1.00	2.00	0
ATOM	1544	O	ASN	157	-10.242	59.489	111.240	1.00	2.00	0
ATOM	1545	N	CYS	158	-9.064	57.962	110.120	1.00	2.00	0
ATOM	1547	CA	CYS	158	-10.074	56.914	110.304	1.00	2.00	0
ATOM	1548	CB	CYS	158	-10.751	56.567	108.970	1.00	2.00	0
ATOM	1549	SG	CYS	158	-11.898	57.864	108.331	1.00	2.00	0
ATOM	1550	C	CYS	158	-9.482	55.665	110.924	1.00	2.00	0
ATOM	1551	O	CYS	158	-10.148	54.648	111.049	1.00	2.00	0
ATOM	1552	N	LEU	159	-8.216	55.772	111.304	1.00	2.00	0
ATOM	1554	CA	LEU	159	-7.433	54.714	111.945	1.00	2.00	0
ATOM	1555	CB	LEU	159	-5.985	55.219	112.037	1.00	2.00	0
ATOM	1556	CG	LEU	159	-4.747	54.363	111.781	1.00	2.00	0
ATOM	1557	CD1	LEU	159	-4.993	53.449	110.617	1.00	2.00	0
ATOM	1558	CD2	LEU	159	-3.536	55.269	111.503	1.00	2.00	0
ATOM	1559	C	LEU	159	-8.010	54.454	113.361	1.00	2.00	0
ATOM	1560	O	LEU	159	-8.548	55.367	113.980	1.00	2.00	0
ATOM	1561	N	PRO	160	-7.951	53.209	113.871	1.00	2.00	0
ATOM	1562	CD	PRO	160	-7.504	51.978	113.208	1.00	2.00	0
ATOM	1563	CA	PRO	160	-8.473	52.896	115.209	1.00	2.00	0
ATOM	1564	CB	PRO	160	-8.398	51.375	115.269	1.00	2.00	0
ATOM	1565	CG	PRO	160	-8.416	50.956	113.838	1.00	2.00	0
ATOM	1566	C	PRO	160	-7.535	53.516	116.228	1.00	2.00	0
ATOM	1567	O	PRO	160	-6.329	53.463	116.031	1.00	2.00	0
ATOM	1568	N	ILE	161	-8.062	54.073	117.315	1.00	10.42	0
ATOM	1570	CA	ILE	161	-7.206	54.717	118.312	1.00	10.42	0
ATOM	1571	CB	ILE	161	-7.862	55.995	118.918	1.00	2.00	0
ATOM	1572	CG2	ILE	161	-8.493	56.837	117.823	1.00	2.00	0
ATOM	1573	CG1	ILE	161	-8.899	55.612	119.987	1.00	2.00	0
ATOM	1574	CD1	ILE	161	-9.428	56.766	120.775	1.00	2.00	0
ATOM	1575	C	ILE	161	-6.741	53.859	119.492	1.00	10.42	0
ATOM	1576	O	ILE	161	-5.808	54.254	120.193	1.00	2.00	0
ATOM	1577	N	ALA	162	-7.387	52.712	119.720	1.00	16.67	0
ATOM	1579	CA	ALA	162	-7.036	51.832	120.837	1.00	16.67	0

ATOM	1580	CB	ALA	162	-7.580	52.409	122.120	1.00	2.00	0
ATOM	1581	C	ALA	162	-7.567	50.414	120.637	1.00	16.67	0
ATOM	1582	O	ALA	162	-8.494	50.203	119.861	1.00	2.00	0
ATOM	1583	N	ALA	163	-6.984	49.455	121.356	1.00	2.00	0
ATOM	1585	CA	ALA	163	-7.379	48.052	121.267	1.00	2.00	0
ATOM	1586	CB	ALA	163	-6.559	47.374	120.197	1.00	14.80	0
ATOM	1587	C	ALA	163	-7.232	47.283	122.604	1.00	2.00	0
ATOM	1588	O	ALA	163	-6.373	47.620	123.425	1.00	8.24	0
ATOM	1589	N	ILE	164	-8.069	46.263	122.813	1.00	8.09	0
ATOM	1591	CA	ILE	164	-8.036	45.424	124.018	1.00	8.09	0
ATOM	1592	CB	ILE	164	-9.323	45.590	124.860	1.00	10.56	0
ATOM	1593	CG2	ILE	164	-9.200	44.830	126.150	1.00	10.56	0
ATOM	1594	CG1	ILE	164	-9.566	47.055	125.187	1.00	10.56	0
ATOM	1595	CD1	ILE	164	-10.886	47.285	125.837	1.00	10.56	0
ATOM	1596	C	ILE	164	-7.910	43.938	123.623	1.00	8.09	0
ATOM	1597	O	ILE	164	-8.866	43.328	123.127	1.00	10.56	0
ATOM	1598	N	VAL	165	-6.739	43.353	123.856	1.00	20.53	0
ATOM	1600	CA	VAL	165	-6.510	41.958	123.503	1.00	21.83	0
ATOM	1601	CB	VAL	165	-5.041	41.664	123.243	1.00	2.00	0
ATOM	1602	CG1	VAL	165	-4.905	40.241	122.717	1.00	2.00	0
ATOM	1603	CG2	VAL	165	-4.460	42.686	122.273	1.00	2.00	0
ATOM	1604	C	VAL	165	-6.973	40.987	124.570	1.00	22.04	0
ATOM	1605	O	VAL	165	-6.546	41.064	125.728	1.00	2.00	0
ATOM	1606	N	ASP	166	-7.841	40.066	124.163	1.00	10.50	0
ATOM	1608	CA	ASP	166	-8.401	39.057	125.046	1.00	16.73	0
ATOM	1609	CB	ASP	166	-7.348	37.980	125.337	1.00	24.26	0
ATOM	1610	CG	ASP	166	-7.245	36.914	124.212	1.00	24.02	0
ATOM	1611	OD1	ASP	166	-8.258	36.207	123.944	1.00	22.19	0
ATOM	1612	OD2	ASP	166	-6.145	36.776	123.611	1.00	26.91	0
ATOM	1613	C	ASP	166	-8.963	39.674	126.326	1.00	15.15	0
ATOM	1614	O	ASP	166	-9.139	39.006	127.336	1.00	12.89	0
ATOM	1615	N	GLU	167	-9.262	40.967	126.231	1.00	2.00	0
ATOM	1617	CA	GLU	167	-9.833	41.811	127.289	1.00	2.00	0
ATOM	1618	CB	GLU	167	-11.280	41.394	127.555	1.00	83.32	0
ATOM	1619	CG	GLU	167	-12.129	41.397	126.273	1.00	2.00	0
ATOM	1620	CD	GLU	167	-11.819	42.603	125.305	1.00	2.00	0
ATOM	1621	OE1	GLU	167	-11.133	42.398	124.242	1.00	2.00	0
ATOM	1622	OE2	GLU	167	-12.268	43.750	125.622	1.00	2.00	0
ATOM	1623	C	GLU	167	-9.056	41.981	128.585	1.00	2.00	0
ATOM	1624	O	GLU	167	-9.634	42.138	129.657	1.00	74.79	0
ATOM	1625	N	LYS	168	-7.733	41.984	128.460	1.00	22.77	0
ATOM	1627	CA	LYS	168	-6.829	42.154	129.589	1.00	14.49	0
ATOM	1628	CB	LYS	168	-6.098	40.844	129.910	1.00	21.81	0
ATOM	1629	CG	LYS	168	-6.956	39.798	130.600	1.00	17.49	0
ATOM	1630	CD	LYS	168	-7.677	40.404	131.802	1.00	18.27	0
ATOM	1631	CE	LYS	168	-8.654	39.411	132.466	1.00	26.28	0
ATOM	1632	NZ	LYS	168	-9.658	40.080	133.373	1.00	29.04	0
ATOM	1636	C	LYS	168	-5.811	43.225	129.237	1.00	11.04	0
ATOM	1637	O	LYS	168	-5.665	44.214	129.947	1.00	17.06	0
ATOM	1638	N	ILE	169	-5.109	43.015	128.131	1.00	2.00	0
ATOM	1640	CA	ILE	169	-4.093	43.950	127.663	1.00	2.00	0
ATOM	1641	CB	ILE	169	-3.151	43.267	126.648	1.00	2.00	0
ATOM	1642	CG2	ILE	169	-1.989	44.184	126.302	1.00	2.00	0
ATOM	1643	CG1	ILE	169	-2.632	41.952	127.215	1.00	2.00	0
ATOM	1644	CD1	ILE	169	-1.691	41.218	126.297	1.00	2.00	0
ATOM	1645	C	ILE	169	-4.731	45.144	126.964	1.00	2.00	0
ATOM	1646	O	ILE	169	-5.393	44.973	125.938	1.00	2.00	0
ATOM	1647	N	PHE	170	-4.572	46.337	127.524	1.00	17.81	0
ATOM	1649	CA	PHE	170	-5.110	47.525	126.877	1.00	19.78	0
ATOM	1650	CB	PHE	170	-5.486	48.610	127.885	1.00	2.00	0
ATOM	1651	CG	PHE	170	-5.895	49.920	127.252	1.00	2.00	0
ATOM	1652	CD1	PHE	170	-7.095	50.028	126.538	1.00	2.00	0
ATOM	1653	CD2	PHE	170	-5.092	51.056	127.390	1.00	2.00	0
ATOM	1654	CE1	PHE	170	-7.493	51.248	125.976	1.00	2.00	0
ATOM	1655	CE2	PHE	170	-5.473	52.282	126.836	1.00	2.00	0
ATOM	1656	CZ	PHE	170	-6.680	52.377	126.127	1.00	2.00	0
ATOM	1657	C	PHE	170	-3.943	47.992	126.038	1.00	23.45	0
ATOM	1658	O	PHE	170	-2.809	47.983	126.518	1.00	2.00	0

ATOM	1659	N	CYS	171	-4.208	48.375	124.790	1.00	2.00	0
ATOM	1661	CA	CYS	171	-3.158	48.836	123.898	1.00	2.00	0
ATOM	1662	CB	CYS	171	-2.952	47.843	122.766	1.00	26.14	0
ATOM	1663	SG	CYS	171	-2.524	46.203	123.305	1.00	16.13	0
ATOM	1664	C	CYS	171	-3.499	50.189	123.310	1.00	2.00	0
ATOM	1665	O	CYS	171	-4.652	50.453	122.943	1.00	26.14	0
ATOM	1666	N	CYS	172	-2.495	51.058	123.265	1.00	2.00	0
ATOM	1668	CA	CYS	172	-2.635	52.378	122.668	1.00	2.00	0
ATOM	1669	CB	CYS	172	-3.403	53.356	123.597	1.00	14.54	0
ATOM	1670	SG	CYS	172	-2.593	53.995	125.094	1.00	15.67	0
ATOM	1671	C	CYS	172	-1.231	52.890	122.287	1.00	2.00	0
ATOM	1672	O	CYS	172	-0.227	52.277	122.657	1.00	7.48	0
ATOM	1673	N	HIS	173	-1.154	53.951	121.488	1.00	2.00	0
ATOM	1675	CA	HIS	173	0.146	54.461	121.112	1.00	2.00	0
ATOM	1676	C	HIS	173	0.815	55.130	122.297	1.00	2.00	0
ATOM	1677	O	HIS	173	1.893	54.707	122.722	1.00	2.00	0
ATOM	1678	CB	HIS	173	0.056	55.457	119.944	1.00	2.00	0
ATOM	1679	CG	HIS	173	1.377	56.074	119.588	1.00	2.00	0
ATOM	1680	ND1	HIS	173	2.487	55.347	119.234	1.00	2.00	0
ATOM	1682	CD2	HIS	173	1.774	57.372	119.585	1.00	2.00	0
ATOM	1683	NE2	HIS	173	3.123	57.441	119.241	1.00	2.00	0
ATOM	1684	CE1	HIS	173	3.492	56.189	119.045	1.00	2.00	0
ATOM	1685	N	GLY	174	0.168	56.172	122.817	1.00	2.00	0
ATOM	1687	CA	GLY	174	0.711	56.933	123.935	1.00	2.00	0
ATOM	1688	C	GLY	174	0.568	56.450	125.386	1.00	2.00	0
ATOM	1689	O	GLY	174	1.556	56.111	126.041	1.00	2.00	0
ATOM	1690	N	GLY	175	-0.648	56.453	125.913	1.00	16.98	0
ATOM	1692	CA	GLY	175	-0.830	56.028	127.283	1.00	16.98	0
ATOM	1693	C	GLY	175	-2.227	56.343	127.763	1.00	16.98	0
ATOM	1694	O	GLY	175	-3.190	56.231	126.999	1.00	66.77	0
ATOM	1695	N	LEU	176	-2.341	56.764	129.021	1.00	11.28	0
ATOM	1697	CA	LEU	176	-3.637	57.063	129.604	1.00	11.28	0
ATOM	1698	CB	LEU	176	-3.740	56.427	130.976	1.00	2.00	0
ATOM	1699	CG	LEU	176	-3.443	54.934	130.966	1.00	2.00	0
ATOM	1700	CD1	LEU	176	-3.469	54.407	132.374	1.00	2.00	0
ATOM	1701	CD2	LEU	176	-4.463	54.218	130.121	1.00	2.00	0
ATOM	1702	C	LEU	176	-3.876	58.545	129.692	1.00	11.28	0
ATOM	1703	O	LEU	176	-2.943	59.329	129.645	1.00	2.00	0
ATOM	1704	N	SER	177	-5.138	58.913	129.850	1.00	6.18	0
ATOM	1706	CA	SER	177	-5.567	60.304	129.918	1.00	6.86	0
ATOM	1707	CB	SER	177	-6.476	60.587	128.718	1.00	12.19	0
ATOM	1708	OG	SER	177	-7.189	61.804	128.835	1.00	12.19	0
ATOM	1710	C	SER	177	-6.356	60.573	131.193	1.00	7.79	0
ATOM	1711	O	SER	177	-7.170	59.749	131.606	1.00	12.19	0
ATOM	1712	N	PRO	178	-6.150	61.736	131.824	1.00	2.00	0
ATOM	1713	CD	PRO	178	-5.223	62.827	131.505	1.00	29.89	0
ATOM	1714	CA	PRO	178	-6.895	62.054	133.041	1.00	2.00	0
ATOM	1715	CB	PRO	178	-6.231	63.337	133.518	1.00	25.57	0
ATOM	1716	CG	PRO	178	-5.842	63.973	132.274	1.00	21.36	0
ATOM	1717	C	PRO	178	-8.394	62.266	132.757	1.00	2.00	0
ATOM	1718	O	PRO	178	-9.140	62.740	133.617	1.00	24.04	0
ATOM	1719	N	ASP	179	-8.821	61.933	131.543	1.00	38.94	0
ATOM	1721	CA	ASP	179	-10.206	62.078	131.129	1.00	37.05	0
ATOM	1722	CB	ASP	179	-10.264	62.870	129.837	1.00	33.34	0
ATOM	1723	CG	ASP	179	-9.964	64.320	130.048	1.00	30.55	0
ATOM	1724	OD1	ASP	179	-10.923	65.045	130.386	1.00	31.71	0
ATOM	1725	OD2	ASP	179	-8.786	64.728	129.889	1.00	32.17	0
ATOM	1726	C	ASP	179	-10.871	60.735	130.923	1.00	40.05	0
ATOM	1727	O	ASP	179	-12.096	60.638	130.873	1.00	34.46	0
ATOM	1728	N	LEU	180	-10.057	59.699	130.791	1.00	15.43	0
ATOM	1730	CA	LEU	180	-10.570	58.362	130.590	1.00	12.98	0
ATOM	1731	CB	LEU	180	-9.446	57.467	130.058	1.00	2.00	0
ATOM	1732	CG	LEU	180	-9.867	56.186	129.338	1.00	2.00	0
ATOM	1733	CD1	LEU	180	-10.706	56.511	128.110	1.00	2.00	0
ATOM	1734	CD2	LEU	180	-8.633	55.413	128.953	1.00	2.00	0
ATOM	1735	C	LEU	180	-11.157	57.806	131.902	1.00	14.43	0
ATOM	1736	O	LEU	180	-10.470	57.709	132.931	1.00	2.00	0
ATOM	1737	N	GLN	181	-12.448	57.492	131.862	1.00	5.88	0

ATOM	1739	CA	GLN	181	-13.184	56.917	132.992	1.00	5.88	0
ATOM	1740	CB	GLN	181	-14.379	57.787	133.375	1.00	32.99	0
ATOM	1741	CG	GLN	181	-14.002	59.152	133.900	1.00	36.07	0
ATOM	1742	CD	GLN	181	-15.101	60.172	133.676	1.00	38.35	0
ATOM	1743	OE1	GLN	181	-16.285	59.886	133.877	1.00	41.53	0
ATOM	1744	NE2	GLN	181	-14.717	61.366	133.242	1.00	38.39	0
ATOM	1747	C	GLN	181	-13.672	55.563	132.500	1.00	5.88	0
ATOM	1748	O	GLN	181	-13.572	54.554	133.205	1.00	24.31	0
ATOM	1749	N	SER	182	-14.188	55.544	131.274	1.00	2.20	0
ATOM	1751	CA	SER	182	-14.651	54.310	130.664	1.00	9.71	0
ATOM	1752	CB	SER	182	-16.174	54.255	130.614	1.00	15.80	0
ATOM	1753	OG	SER	182	-16.668	54.856	129.433	1.00	17.25	0
ATOM	1755	C	SER	182	-14.112	54.177	129.248	1.00	3.77	0
ATOM	1756	O	SER	182	-13.359	55.019	128.751	1.00	15.80	0
ATOM	1757	N	MET	183	-14.526	53.091	128.615	1.00	2.00	0
ATOM	1759	CA	MET	183	-14.156	52.780	127.251	1.00	2.00	0
ATOM	1760	CB	MET	183	-14.100	51.272	127.064	1.00	2.00	0
ATOM	1761	CG	MET	183	-13.171	50.616	128.048	1.00	2.00	0
ATOM	1762	SD	MET	183	-11.620	51.473	128.022	1.00	2.00	0
ATOM	1763	CE	MET	183	-10.520	50.135	127.900	1.00	2.00	0
ATOM	1764	C	MET	183	-15.204	53.373	126.326	1.00	2.00	0
ATOM	1765	O	MET	183	-14.959	53.550	125.129	1.00	2.00	0
ATOM	1766	N	GLU	184	-16.370	53.700	126.882	1.00	2.00	0
ATOM	1768	CA	GLU	184	-17.432	54.280	126.082	1.00	2.00	0
ATOM	1769	CB	GLU	184	-18.668	54.531	126.910	1.00	6.25	0
ATOM	1770	CG	GLU	184	-19.830	54.977	126.073	1.00	8.82	0
ATOM	1771	CD	GLU	184	-20.273	53.927	125.068	1.00	13.01	0
ATOM	1772	OE1	GLU	184	-19.846	52.744	125.181	1.00	14.09	0
ATOM	1773	OE2	GLU	184	-21.064	54.293	124.164	1.00	20.29	0
ATOM	1774	C	GLU	184	-16.978	55.586	125.481	1.00	2.00	0
ATOM	1775	O	GLU	184	-17.399	55.946	124.392	1.00	23.33	0
ATOM	1776	N	GLN	185	-16.117	56.295	126.198	1.00	12.32	0
ATOM	1778	CA	GLN	185	-15.599	57.561	125.714	1.00	14.30	0
ATOM	1779	CB	GLN	185	-14.697	58.190	126.758	1.00	43.49	0
ATOM	1780	CG	GLN	185	-15.454	58.629	127.990	1.00	47.40	0
ATOM	1781	CD	GLN	185	-14.537	58.929	129.139	1.00	49.32	0
ATOM	1782	OE1	GLN	185	-13.994	58.016	129.753	1.00	56.49	0
ATOM	1783	NE2	GLN	185	-14.350	60.208	129.437	1.00	49.76	0
ATOM	1786	C	GLN	185	-14.834	57.307	124.432	1.00	16.93	0
ATOM	1787	O	GLN	185	-14.973	58.053	123.461	1.00	43.79	0
ATOM	1788	N	ILE	186	-14.044	56.238	124.420	1.00	5.67	0
ATOM	1790	CA	ILE	186	-13.280	55.880	123.235	1.00	5.67	0
ATOM	1791	CB	ILE	186	-12.436	54.613	123.470	1.00	16.18	0
ATOM	1792	CG2	ILE	186	-11.675	54.243	122.208	1.00	11.85	0
ATOM	1793	CG1	ILE	186	-11.489	54.825	124.642	1.00	13.18	0
ATOM	1794	CD1	ILE	186	-10.545	55.954	124.459	1.00	17.92	0
ATOM	1795	C	ILE	186	-14.294	55.566	122.143	1.00	5.67	0
ATOM	1796	O	ILE	186	-14.260	56.145	121.060	1.00	19.35	0
ATOM	1797	N	ARG	187	-15.207	54.655	122.471	1.00	17.59	0
ATOM	1799	CA	ARG	187	-16.243	54.205	121.561	1.00	16.33	0
ATOM	1800	CB	ARG	187	-17.141	53.165	122.237	1.00	20.41	0
ATOM	1801	CG	ARG	187	-16.468	51.900	122.723	1.00	29.32	0
ATOM	1802	CD	ARG	187	-17.497	51.006	123.447	1.00	31.43	0
ATOM	1803	NE	ARG	187	-16.888	49.888	124.165	1.00	38.34	0
ATOM	1805	CZ	ARG	187	-16.311	48.838	123.580	1.00	34.30	0
ATOM	1806	NH1	ARG	187	-16.256	48.747	122.252	1.00	41.37	0
ATOM	1809	NH2	ARG	187	-15.783	47.873	124.322	1.00	34.50	0
ATOM	1812	C	ARG	187	-17.148	55.302	121.011	1.00	15.89	0
ATOM	1813	O	ARG	187	-17.937	55.032	120.108	1.00	20.82	0
ATOM	1814	N	ARG	188	-17.071	56.524	121.529	1.00	2.00	0
ATOM	1816	CA	ARG	188	-17.964	57.557	121.012	1.00	2.00	0
ATOM	1817	CB	ARG	188	-18.878	58.105	122.106	1.00	31.38	0
ATOM	1818	CG	ARG	188	-18.184	58.827	123.228	1.00	29.44	0
ATOM	1819	CD	ARG	188	-19.202	59.586	124.034	1.00	31.32	0
ATOM	1820	NE	ARG	188	-20.410	58.802	124.237	1.00	33.18	0
ATOM	1822	CZ	ARG	188	-21.637	59.285	124.112	1.00	29.63	0
ATOM	1823	NH1	ARG	188	-21.827	60.561	123.777	1.00	36.26	0
ATOM	1826	NH2	ARG	188	-22.671	58.484	124.332	1.00	32.06	0

ATOM	1829	C	ARG	188	-17.255	58.682	120.332	1.00	2.00	0
ATOM	1830	O	ARG	188	-17.758	59.804	120.250	1.00	31.89	0
ATOM	1831	N	ILE	189	-16.070	58.369	119.846	1.00	17.06	0
ATOM	1833	CA	ILE	189	-15.263	59.333	119.136	1.00	16.98	0
ATOM	1834	CB	ILE	189	-13.759	59.043	119.345	1.00	16.67	0
ATOM	1835	CG2	ILE	189	-12.924	59.973	118.493	1.00	17.43	0
ATOM	1836	CG1	ILE	189	-13.411	59.205	120.826	1.00	17.65	0
ATOM	1837	CD1	ILE	189	-11.970	58.946	121.173	1.00	16.74	0
ATOM	1838	C	ILE	189	-15.620	59.244	117.656	1.00	19.51	0
ATOM	1839	O	ILE	189	-15.448	58.184	117.044	1.00	25.93	0
ATOM	1840	N	MET	190	-16.158	60.342	117.108	1.00	22.12	0
ATOM	1842	CA	MET	190	-16.514	60.420	115.685	1.00	24.92	0
ATOM	1843	CB	MET	190	-17.051	61.812	115.320	1.00	46.39	0
ATOM	1844	CG	MET	190	-17.366	61.977	113.826	1.00	46.97	0
ATOM	1845	SD	MET	190	-17.820	63.658	113.312	1.00	58.03	0
ATOM	1846	CE	MET	190	-16.271	64.266	112.598	1.00	52.38	0
ATOM	1847	C	MET	190	-15.173	60.194	115.015	1.00	25.36	0
ATOM	1848	O	MET	190	-14.287	61.041	115.106	1.00	32.57	0
ATOM	1849	N	ARG	191	-15.023	59.057	114.346	1.00	2.00	0
ATOM	1851	CA	ARG	191	-13.732	58.738	113.772	1.00	2.00	0
ATOM	1852	CB	ARG	191	-13.731	57.384	113.089	1.00	2.00	0
ATOM	1853	CG	ARG	191	-12.300	56.900	112.821	1.00	11.31	0
ATOM	1854	CD	ARG	191	-11.978	55.799	113.752	1.00	11.31	0
ATOM	1855	NE	ARG	191	-13.139	54.935	113.762	1.00	2.00	0
ATOM	1857	CZ	ARG	191	-13.124	53.663	113.416	1.00	2.00	0
ATOM	1858	NH1	ARG	191	-11.985	53.085	113.047	1.00	2.00	0
ATOM	1861	NH2	ARG	191	-14.263	52.984	113.430	1.00	2.00	0
ATOM	1864	C	ARG	191	-13.084	59.769	112.857	1.00	2.00	0
ATOM	1865	O	ARG	191	-11.995	60.267	113.202	1.00	6.10	0
ATOM	1866	N	PRO	192	-13.685	60.065	111.670	1.00	37.06	0
ATOM	1867	CD	PRO	192	-14.912	59.530	111.045	1.00	2.00	0
ATOM	1868	CA	PRO	192	-13.048	61.068	110.799	1.00	36.28	0
ATOM	1869	CB	PRO	192	-14.114	61.335	109.749	1.00	2.00	0
ATOM	1870	CG	PRO	192	-14.743	59.973	109.602	1.00	2.00	0
ATOM	1871	C	PRO	192	-12.787	62.261	111.693	1.00	37.24	0
ATOM	1872	O	PRO	192	-13.697	63.033	112.004	1.00	2.00	0
ATOM	1873	N	THR	193	-11.552	62.348	112.168	1.00	2.00	0
ATOM	1875	CA	THR	193	-11.182	63.396	113.089	1.00	2.00	0
ATOM	1876	CB	THR	193	-11.627	63.063	114.540	1.00	22.05	0
ATOM	1877	OG1	THR	193	-11.349	64.183	115.392	1.00	31.69	0
ATOM	1879	CG2	THR	193	-10.862	61.859	115.089	1.00	21.46	0
ATOM	1880	C	THR	193	-9.700	63.661	113.152	1.00	2.00	0
ATOM	1881	O	THR	193	-8.865	62.795	112.860	1.00	17.62	0
ATOM	1882	N	ASP	194	-9.394	64.879	113.572	1.00	2.00	0
ATOM	1884	CA	ASP	194	-8.031	65.311	113.744	1.00	2.00	0
ATOM	1885	CB	ASP	194	-7.927	66.805	113.431	1.00	49.25	0
ATOM	1886	CG	ASP	194	-6.561	67.197	112.912	1.00	49.25	0
ATOM	1887	OD1	ASP	194	-6.132	68.334	113.194	1.00	49.25	0
ATOM	1888	OD2	ASP	194	-5.920	66.371	112.217	1.00	49.25	0
ATOM	1889	C	ASP	194	-7.686	65.041	115.216	1.00	2.00	0
ATOM	1890	O	ASP	194	-8.571	64.978	116.077	1.00	54.62	0
ATOM	1891	N	VAL	195	-6.408	64.836	115.488	1.00	17.01	0
ATOM	1893	CA	VAL	195	-5.948	64.611	116.839	1.00	12.88	0
ATOM	1894	CB	VAL	195	-4.509	64.017	116.818	1.00	9.98	0
ATOM	1895	CG1	VAL	195	-3.934	63.875	118.239	1.00	9.98	0
ATOM	1896	CG2	VAL	195	-4.532	62.675	116.124	1.00	9.98	0
ATOM	1897	C	VAL	195	-5.971	65.994	117.511	1.00	12.88	0
ATOM	1898	O	VAL	195	-5.343	66.934	117.038	1.00	9.98	0
ATOM	1899	N	PRO	196	-6.771	66.152	118.567	1.00	16.08	0
ATOM	1900	CD	PRO	196	-7.805	65.214	119.033	1.00	26.02	0
ATOM	1901	CA	PRO	196	-6.862	67.429	119.284	1.00	21.91	0
ATOM	1902	CB	PRO	196	-8.026	67.195	120.240	1.00	25.86	0
ATOM	1903	CG	PRO	196	-8.874	66.153	119.496	1.00	25.31	0
ATOM	1904	C	PRO	196	-5.560	67.735	120.027	1.00	24.64	0
ATOM	1905	O	PRO	196	-4.809	66.818	120.349	1.00	23.54	0
ATOM	1906	N	ASP	197	-5.291	69.010	120.302	1.00	39.93	0
ATOM	1908	CA	ASP	197	-4.058	69.377	121.005	1.00	38.76	0
ATOM	1909	CB	ASP	197	-3.605	70.789	120.612	1.00	78.93	0

ATOM	1910	CG	ASP	197	-4.726	71.800	120.658	1.00	84.50	0
ATOM	1911	OD1	ASP	197	-5.071	72.263	121.768	1.00	83.41	0
ATOM	1912	OD2	ASP	197	-5.258	72.134	119.578	1.00	90.03	0
ATOM	1913	C	ASP	197	-4.162	69.256	122.520	1.00	41.84	0
ATOM	1914	O	ASP	197	-3.227	69.577	123.255	1.00	85.35	0
ATOM	1915	N	GLN	198	-5.316	68.789	122.973	1.00	2.00	0
ATOM	1917	CA	GLN	198	-5.581	68.588	124.385	1.00	2.00	0
ATOM	1918	CB	GLN	198	-5.686	69.937	125.120	1.00	27.32	0
ATOM	1919	CG	GLN	198	-6.621	70.967	124.503	1.00	32.39	0
ATOM	1920	CD	GLN	198	-7.981	71.041	125.192	1.00	29.94	0
ATOM	1921	OE1	GLN	198	-8.108	70.793	126.397	1.00	32.81	0
ATOM	1922	NE2	GLN	198	-9.007	71.391	124.424	1.00	29.42	0
ATOM	1925	C	GLN	198	-6.863	67.793	124.492	1.00	2.00	0
ATOM	1926	O	GLN	198	-7.748	67.909	123.640	1.00	26.90	0
ATOM	1927	N	GLY	199	-6.943	66.949	125.509	1.00	15.20	0
ATOM	1929	CA	GLY	199	-8.137	66.148	125.692	1.00	15.56	0
ATOM	1930	C	GLY	199	-7.820	64.670	125.631	1.00	13.32	0
ATOM	1931	O	GLY	199	-6.655	64.283	125.502	1.00	2.00	0
ATOM	1932	N	LEU	200	-8.857	63.842	125.684	1.00	2.00	0
ATOM	1934	CA	LEU	200	-8.690	62.402	125.666	1.00	2.00	0
ATOM	1935	CB	LEU	200	-10.049	61.701	125.667	1.00	2.00	0
ATOM	1936	CG	LEU	200	-9.945	60.224	126.081	1.00	2.00	0
ATOM	1937	CD1	LEU	200	-11.126	59.800	126.947	1.00	2.00	0
ATOM	1938	CD2	LEU	200	-9.842	59.380	124.847	1.00	2.00	0
ATOM	1939	C	LEU	200	-7.850	61.875	124.521	1.00	2.00	0
ATOM	1940	O	LEU	200	-6.764	61.323	124.764	1.00	2.00	0
ATOM	1941	N	LEU	201	-8.344	62.045	123.283	1.00	2.00	0
ATOM	1943	CA	LEU	201	-7.663	61.566	122.070	1.00	2.00	0
ATOM	1944	CB	LEU	201	-8.378	62.041	120.811	1.00	2.00	0
ATOM	1945	CG	LEU	201	-8.369	61.100	119.589	1.00	2.00	0
ATOM	1946	CD1	LEU	201	-8.895	61.855	118.375	1.00	2.00	0
ATOM	1947	CD2	LEU	201	-6.981	60.569	119.277	1.00	2.00	0
ATOM	1948	C	LEU	201	-6.246	62.078	122.059	1.00	2.00	0
ATOM	1949	O	LEU	201	-5.319	61.347	121.715	1.00	2.00	0
ATOM	1950	N	CYS	202	-6.071	63.333	122.446	1.00	2.00	0
ATOM	1952	CA	CYS	202	-4.733	63.891	122.484	1.00	2.00	0
ATOM	1953	CB	CYS	202	-4.722	65.306	123.024	1.00	2.00	0
ATOM	1954	SG	CYS	202	-3.012	65.850	123.209	1.00	2.00	0
ATOM	1955	C	CYS	202	-3.850	63.076	123.394	1.00	2.00	0
ATOM	1956	O	CYS	202	-2.719	62.715	123.036	1.00	2.00	0
ATOM	1957	N	ASP	203	-4.385	62.798	124.584	1.00	15.07	0
ATOM	1959	CA	ASP	203	-3.673	62.057	125.611	1.00	11.86	0
ATOM	1960	CB	ASP	203	-4.429	62.142	126.931	1.00	13.71	0
ATOM	1961	CG	ASP	203	-4.449	63.538	127.497	1.00	15.77	0
ATOM	1962	OD1	ASP	203	-3.529	64.315	127.162	1.00	11.73	0
ATOM	1963	OD2	ASP	203	-5.380	63.861	128.271	1.00	16.16	0
ATOM	1964	C	ASP	203	-3.369	60.615	125.262	1.00	13.81	0
ATOM	1965	O	ASP	203	-2.254	60.155	125.492	1.00	23.94	0
ATOM	1966	N	LEU	204	-4.330	59.902	124.695	1.00	10.49	0
ATOM	1968	CA	LEU	204	-4.097	58.509	124.332	1.00	10.49	0
ATOM	1969	CB	LEU	204	-5.351	57.912	123.717	1.00	10.22	0
ATOM	1970	CG	LEU	204	-6.478	57.606	124.696	1.00	10.22	0
ATOM	1971	CD1	LEU	204	-7.667	57.281	123.866	1.00	10.22	0
ATOM	1972	CD2	LEU	204	-6.143	56.441	125.620	1.00	10.22	0
ATOM	1973	C	LEU	204	-2.930	58.347	123.361	1.00	10.49	0
ATOM	1974	O	LEU	204	-2.204	57.352	123.392	1.00	10.22	0
ATOM	1975	N	LEU	205	-2.748	59.336	122.501	1.00	2.00	0
ATOM	1977	CA	LEU	205	-1.679	59.301	121.525	1.00	2.00	0
ATOM	1978	CB	LEU	205	-2.161	59.933	120.219	1.00	2.00	0
ATOM	1979	CG	LEU	205	-3.459	59.463	119.551	1.00	2.00	0
ATOM	1980	CD1	LEU	205	-3.595	60.238	118.259	1.00	2.00	0
ATOM	1981	CD2	LEU	205	-3.459	57.954	119.269	1.00	2.00	0
ATOM	1982	C	LEU	205	-0.409	60.018	121.967	1.00	2.00	0
ATOM	1983	O	LEU	205	0.620	59.890	121.314	1.00	2.00	0
ATOM	1984	N	TRP	206	-0.472	60.756	123.072	1.00	10.02	0
ATOM	1986	CA	TRP	206	0.678	61.526	123.545	1.00	10.02	0
ATOM	1987	CB	TRP	206	0.362	62.994	123.408	1.00	2.00	0
ATOM	1988	CG	TRP	206	0.413	63.485	122.052	1.00	2.00	0

ATOM	1989	CD2	TRP	206	1.532	64.103	121.420	1.00	2.00	0
ATOM	1990	CE2	TRP	206	1.105	64.535	120.148	1.00	2.00	0
ATOM	1991	CE3	TRP	206	2.854	64.355	121.813	1.00	2.00	0
ATOM	1992	CD1	TRP	206	-0.616	63.541	121.162	1.00	2.00	0
ATOM	1993	NE1	TRP	206	-0.212	64.178	120.017	1.00	2.00	0
ATOM	1995	CZ2	TRP	206	1.950	65.207	119.263	1.00	2.00	0
ATOM	1996	CZ3	TRP	206	3.697	65.024	120.932	1.00	2.00	0
ATOM	1997	CH2	TRP	206	3.238	65.443	119.669	1.00	2.00	0
ATOM	1998	C	TRP	206	1.246	61.330	124.955	1.00	10.02	0
ATOM	1999	O	TRP	206	2.419	61.639	125.194	1.00	2.00	0
ATOM	2000	N	SER	207	0.418	60.867	125.886	1.00	2.00	0
ATOM	2002	CA	SER	207	0.830	60.690	127.267	1.00	2.00	0
ATOM	2003	CB	SER	207	-0.363	60.273	128.121	1.00	29.76	0
ATOM	2004	OG	SER	207	-0.482	61.120	129.256	1.00	35.73	0
ATOM	2006	C	SER	207	1.951	59.699	127.446	1.00	2.00	0
ATOM	2007	O	SER	207	2.075	58.743	126.681	1.00	31.05	0
ATOM	2008	N	ASP	208	2.777	59.943	128.462	1.00	2.00	0
ATOM	2010	CA	ASP	208	3.899	59.056	128.764	1.00	2.00	0
ATOM	2011	CB	ASP	208	5.257	59.714	128.505	1.00	42.39	0
ATOM	2012	CG	ASP	208	5.296	60.532	127.256	1.00	46.59	0
ATOM	2013	OD1	ASP	208	5.695	61.706	127.362	1.00	48.93	0
ATOM	2014	OD2	ASP	208	4.959	60.008	126.180	1.00	44.70	0
ATOM	2015	C	ASP	208	3.903	58.705	130.231	1.00	2.00	0
ATOM	2016	O	ASP	208	3.580	59.537	131.072	1.00	45.54	0
ATOM	2017	N	PRO	209	4.244	57.457	130.559	1.00	10.98	0
ATOM	2018	CD	PRO	209	4.509	56.316	129.673	1.00	2.00	0
ATOM	2019	CA	PRO	209	4.299	57.040	131.957	1.00	10.98	0
ATOM	2020	CB	PRO	209	4.407	55.522	131.845	1.00	2.00	0
ATOM	2021	CG	PRO	209	5.197	55.356	130.604	1.00	2.00	0
ATOM	2022	C	PRO	209	5.584	57.675	132.507	1.00	10.98	0
ATOM	2023	O	PRO	209	6.448	58.078	131.712	1.00	2.00	0
ATOM	2024	N	ASP	210	5.724	57.774	133.833	1.00	2.00	0
ATOM	2026	CA	ASP	210	6.931	58.360	134.413	1.00	2.00	0
ATOM	2027	CB	ASP	210	6.755	59.863	134.614	1.00	31.00	0
ATOM	2028	CG	ASP	210	8.050	60.570	134.990	1.00	36.69	0
ATOM	2029	OD1	ASP	210	9.132	59.956	134.874	1.00	33.32	0
ATOM	2030	OD2	ASP	210	7.989	61.756	135.396	1.00	38.93	0
ATOM	2031	C	ASP	210	7.304	57.734	135.729	1.00	2.00	0
ATOM	2032	O	ASP	210	6.448	57.320	136.496	1.00	28.60	0
ATOM	2033	N	LYS	211	8.608	57.666	135.966	1.00	4.23	0
ATOM	2035	CA	LYS	211	9.170	57.136	137.211	1.00	9.37	0
ATOM	2036	CB	LYS	211	10.647	56.760	137.024	1.00	17.66	0
ATOM	2037	CG	LYS	211	10.941	55.441	136.345	1.00	29.60	0
ATOM	2038	CD	LYS	211	12.451	55.184	136.403	1.00	32.82	0
ATOM	2039	CE	LYS	211	12.852	53.831	135.809	1.00	42.70	0
ATOM	2040	NZ	LYS	211	14.336	53.616	135.852	1.00	41.45	0
ATOM	2044	C	LYS	211	9.100	58.157	138.367	1.00	7.69	0
ATOM	2045	O	LYS	211	8.746	57.803	139.481	1.00	18.85	0
ATOM	2046	N	ASP	212	9.456	59.414	138.093	1.00	2.00	0
ATOM	2048	CA	ASP	212	9.468	60.483	139.101	1.00	2.00	0
ATOM	2049	CB	ASP	212	10.322	61.669	138.624	1.00	39.78	0
ATOM	2050	CG	ASP	212	11.483	61.254	137.754	1.00	46.31	0
ATOM	2051	OD1	ASP	212	11.823	62.030	136.834	1.00	41.85	0
ATOM	2052	OD2	ASP	212	12.051	60.166	137.987	1.00	46.28	0
ATOM	2053	C	ASP	212	8.074	61.033	139.412	1.00	2.00	0
ATOM	2054	O	ASP	212	7.943	62.164	139.903	1.00	41.82	0
ATOM	2055	N	VAL	213	7.040	60.250	139.124	1.00	2.00	0
ATOM	2057	CA	VAL	213	5.669	60.690	139.340	1.00	2.00	0
ATOM	2058	CB	VAL	213	5.137	61.376	138.050	1.00	2.00	0
ATOM	2059	CG1	VAL	213	3.652	61.247	137.922	1.00	2.00	0
ATOM	2060	CG2	VAL	213	5.505	62.826	138.076	1.00	2.00	0
ATOM	2061	C	VAL	213	4.767	59.526	139.763	1.00	2.00	0
ATOM	2062	O	VAL	213	5.007	58.356	139.390	1.00	2.00	0
ATOM	2063	N	LEU	214	3.748	59.844	140.564	1.00	21.53	0
ATOM	2065	CA	LEU	214	2.815	58.830	141.022	1.00	19.34	0
ATOM	2066	CB	LEU	214	2.742	58.809	142.543	1.00	14.66	0
ATOM	2067	CG	LEU	214	2.371	57.438	143.097	1.00	15.86	0
ATOM	2068	CD1	LEU	214	3.507	56.477	142.816	1.00	9.71	0

ATOM	2069	CD2	LEU	214	2.109	57.530	144.588	1.00	17.44	0
ATOM	2070	C	LEU	214	1.433	59.068	140.439	1.00	19.87	0
ATOM	2071	O	LEU	214	0.757	58.124	140.033	1.00	9.54	0
ATOM	2072	N	GLY	215	1.003	60.322	140.411	1.00	16.98	0
ATOM	2074	CA	GLY	215	-0.299	60.640	139.852	1.00	11.19	0
ATOM	2075	C	GLY	215	-0.081	61.255	138.487	1.00	12.07	0
ATOM	2076	O	GLY	215	0.772	60.796	137.739	1.00	10.02	0
ATOM	2077	N	TRP	216	-0.824	62.303	138.167	1.00	2.00	0
ATOM	2079	CA	TRP	216	-0.684	62.979	136.890	1.00	2.00	0
ATOM	2080	CB	TRP	216	-2.030	63.535	136.458	1.00	2.00	0
ATOM	2081	CG	TRP	216	-2.903	62.452	136.050	1.00	2.00	0
ATOM	2082	CD2	TRP	216	-2.840	61.741	134.804	1.00	2.00	0
ATOM	2083	CE2	TRP	216	-3.806	60.713	134.865	1.00	2.00	0
ATOM	2084	CE3	TRP	216	-2.050	61.865	133.648	1.00	2.00	0
ATOM	2085	CD1	TRP	216	-3.879	61.860	136.789	1.00	2.00	0
ATOM	2086	NE1	TRP	216	-4.425	60.811	136.087	1.00	2.00	0
ATOM	2088	CZ2	TRP	216	-4.005	59.812	133.809	1.00	2.00	0
ATOM	2089	CZ3	TRP	216	-2.251	60.970	132.605	1.00	2.00	0
ATOM	2090	CH2	TRP	216	-3.217	59.961	132.695	1.00	2.00	0
ATOM	2091	C	TRP	216	0.310	64.101	136.985	1.00	2.00	0
ATOM	2092	O	TRP	216	0.261	64.883	137.926	1.00	2.00	0
ATOM	2093	N	GLY	217	1.213	64.182	136.021	1.00	12.63	0
ATOM	2095	CA	GLY	217	2.199	65.245	136.028	1.00	15.52	0
ATOM	2096	C	GLY	217	2.312	65.928	134.675	1.00	10.15	0
ATOM	2097	O	GLY	217	1.627	65.559	133.720	1.00	26.84	0
ATOM	2098	N	GLU	218	3.189	66.923	134.594	1.00	23.86	0
ATOM	2100	CA	GLU	218	3.434	67.686	133.364	1.00	22.47	0
ATOM	2101	CB	GLU	218	4.198	68.978	133.729	1.00	65.82	0
ATOM	2102	CG	GLU	218	5.082	69.595	132.641	1.00	67.96	0
ATOM	2103	CD	GLU	218	6.577	69.562	132.987	1.00	67.00	0
ATOM	2104	OE1	GLU	218	7.056	70.519	133.631	1.00	68.41	0
ATOM	2105	OE2	GLU	218	7.276	68.589	132.616	1.00	63.29	0
ATOM	2106	C	GLU	218	4.232	66.841	132.371	1.00	25.48	0
ATOM	2107	O	GLU	218	4.808	65.820	132.750	1.00	67.07	0
ATOM	2108	N	ASN	219	4.253	67.245	131.103	1.00	21.19	0
ATOM	2110	CA	ASN	219	5.039	66.510	130.108	1.00	21.18	0
ATOM	2111	CB	ASN	219	4.140	65.888	129.048	1.00	10.60	0
ATOM	2112	CG	ASN	219	4.832	64.791	128.282	1.00	14.78	0
ATOM	2113	OD1	ASN	219	6.052	64.646	128.341	1.00	9.20	0
ATOM	2114	ND2	ASN	219	4.057	64.003	127.560	1.00	8.28	0
ATOM	2117	C	ASN	219	6.058	67.411	129.425	1.00	21.70	0
ATOM	2118	O	ASN	219	5.776	68.576	129.151	1.00	9.52	0
ATOM	2119	N	ASP	220	7.246	66.886	129.151	1.00	35.32	0
ATOM	2121	CA	ASP	220	8.266	67.690	128.485	1.00	34.19	0
ATOM	2122	CB	ASP	220	9.585	66.900	128.358	1.00	48.55	0
ATOM	2123	CG	ASP	220	9.469	65.673	127.447	1.00	92.38	0
ATOM	2124	OD1	ASP	220	9.083	64.584	127.938	1.00	48.43	0
ATOM	2125	OD2	ASP	220	9.778	65.797	126.237	1.00	92.09	0
ATOM	2126	C	ASP	220	7.763	68.148	127.100	1.00	33.44	0
ATOM	2127	O	ASP	220	8.045	69.262	126.661	1.00	47.84	0
ATOM	2128	N	ARG	221	6.986	67.287	126.444	1.00	22.98	0
ATOM	2130	CA	ARG	221	6.427	67.552	125.127	1.00	22.11	0
ATOM	2131	CB	ARG	221	5.578	66.382	124.672	1.00	2.00	0
ATOM	2132	CG	ARG	221	6.251	65.056	124.739	1.00	2.00	0
ATOM	2133	CD	ARG	221	5.241	63.981	124.421	1.00	2.00	0
ATOM	2134	NE	ARG	221	5.828	62.658	124.590	1.00	2.00	0
ATOM	2136	CZ	ARG	221	6.785	62.154	123.811	1.00	2.00	0
ATOM	2137	NH1	ARG	221	7.255	62.866	122.790	1.00	2.00	0
ATOM	2140	NH2	ARG	221	7.285	60.947	124.064	1.00	2.00	0
ATOM	2143	C	ARG	221	5.546	68.776	125.109	1.00	18.96	0
ATOM	2144	O	ARG	221	5.164	69.239	124.052	1.00	2.00	0
ATOM	2145	N	GLY	222	5.188	69.280	126.280	1.00	2.00	0
ATOM	2147	CA	GLY	222	4.328	70.447	126.343	1.00	2.00	0
ATOM	2148	C	GLY	222	2.939	70.103	125.844	1.00	2.00	0
ATOM	2149	O	GLY	222	2.142	70.988	125.509	1.00	29.15	0
ATOM	2150	N	VAL	223	2.658	68.804	125.776	1.00	2.00	0
ATOM	2152	CA	VAL	223	1.356	68.313	125.342	1.00	2.00	0
ATOM	2153	CB	VAL	223	1.364	67.860	123.839	1.00	2.00	0

ATOM	2154	CG1	VAL	223	-0.063	67.888	123.280	1.00	2.00	0
ATOM	2155	CG2	VAL	223	2.258	68.762	123.004	1.00	2.00	0
ATOM	2156	C	VAL	223	1.071	67.125	126.250	1.00	2.00	0
ATOM	2157	O	VAL	223	2.004	66.431	126.656	1.00	2.00	0
ATOM	2158	N	SER	224	-0.205	66.897	126.550	1.00	12.21	0
ATOM	2160	CA	SER	224	-0.661	65.825	127.440	1.00	15.55	0
ATOM	2161	CB	SER	224	-0.609	64.453	126.759	1.00	6.64	0
ATOM	2162	OG	SER	224	0.713	64.003	126.546	1.00	10.80	0
ATOM	2164	C	SER	224	0.077	65.779	128.787	1.00	20.53	0
ATOM	2165	O	SER	224	0.814	66.706	129.153	1.00	8.42	0
ATOM	2166	N	PHE	225	-0.124	64.700	129.533	1.00	6.68	0
ATOM	2168	CA	PHE	225	0.484	64.586	130.839	1.00	6.68	0
ATOM	2169	CB	PHE	225	-0.625	64.489	131.890	1.00	14.03	0
ATOM	2170	CG	PHE	225	-1.670	65.552	131.758	1.00	11.21	0
ATOM	2171	CD1	PHE	225	-2.925	65.248	131.239	1.00	11.66	0
ATOM	2172	CD2	PHE	225	-1.396	66.869	132.131	1.00	11.41	0
ATOM	2173	CE1	PHE	225	-3.899	66.241	131.086	1.00	11.76	0
ATOM	2174	CE2	PHE	225	-2.363	67.869	131.983	1.00	14.72	0
ATOM	2175	CZ	PHE	225	-3.618	67.553	131.458	1.00	16.73	0
ATOM	2176	C	PHE	225	1.405	63.392	130.957	1.00	6.68	0
ATOM	2177	O	PHE	225	1.902	62.850	129.966	1.00	15.31	0
ATOM	2178	N	THR	226	1.663	63.022	132.203	1.00	2.00	0
ATOM	2180	CA	THR	226	2.473	61.872	132.509	1.00	2.00	0
ATOM	2181	CB	THR	226	3.898	62.226	132.853	1.00	13.51	0
ATOM	2182	OG1	THR	226	4.607	61.012	133.094	1.00	13.51	0
ATOM	2184	CG2	THR	226	3.961	63.081	134.086	1.00	13.51	0
ATOM	2185	C	THR	226	1.809	61.217	133.686	1.00	2.00	0
ATOM	2186	O	THR	226	1.039	61.861	134.394	1.00	13.51	0
ATOM	2187	N	PHE	227	2.086	59.938	133.883	1.00	2.00	0
ATOM	2189	CA	PHE	227	1.466	59.191	134.957	1.00	2.00	0
ATOM	2190	CB	PHE	227	0.206	58.448	134.472	1.00	18.74	0
ATOM	2191	CG	PHE	227	0.362	57.793	133.131	1.00	21.51	0
ATOM	2192	CD1	PHE	227	0.717	56.453	133.034	1.00	18.55	0
ATOM	2193	CD2	PHE	227	0.188	58.532	131.954	1.00	20.45	0
ATOM	2194	CE1	PHE	227	0.902	55.857	131.787	1.00	19.97	0
ATOM	2195	CE2	PHE	227	0.371	57.948	130.698	1.00	14.44	0
ATOM	2196	CZ	PHE	227	0.729	56.612	130.612	1.00	17.09	0
ATOM	2197	C	PHE	227	2.427	58.224	135.562	1.00	2.00	0
ATOM	2198	O	PHE	227	3.282	57.668	134.888	1.00	20.11	0
ATOM	2199	N	GLY	228	2.294	58.066	136.867	1.00	21.90	0
ATOM	2201	CA	GLY	228	3.143	57.165	137.607	1.00	20.86	0
ATOM	2202	C	GLY	228	2.424	55.859	137.815	1.00	24.57	0
ATOM	2203	O	GLY	228	1.365	55.615	137.223	1.00	2.00	0
ATOM	2204	N	ALA	229	2.974	55.041	138.704	1.00	2.00	0
ATOM	2206	CA	ALA	229	2.422	53.722	138.971	1.00	2.00	0
ATOM	2207	CB	ALA	229	3.372	52.924	139.835	1.00	2.00	0
ATOM	2208	C	ALA	229	1.055	53.706	139.576	1.00	2.00	0
ATOM	2209	O	ALA	229	0.359	52.705	139.460	1.00	2.00	0
ATOM	2210	N	GLU	230	0.666	54.802	140.220	1.00	2.00	0
ATOM	2212	CA	GLU	230	-0.648	54.881	140.875	1.00	2.00	0
ATOM	2213	CB	GLU	230	-0.787	56.193	141.647	1.00	66.07	0
ATOM	2214	CG	GLU	230	-1.123	56.014	143.111	1.00	71.18	0
ATOM	2215	CD	GLU	230	-2.376	55.175	143.337	1.00	2.00	0
ATOM	2216	OE1	GLU	230	-2.275	53.918	143.199	1.00	2.00	0
ATOM	2217	OE2	GLU	230	-3.448	55.773	143.663	1.00	2.00	0
ATOM	2218	C	GLU	230	-1.769	54.777	139.862	1.00	2.00	0
ATOM	2219	O	GLU	230	-2.649	53.922	139.966	1.00	60.28	0
ATOM	2220	N	VAL	231	-1.684	55.652	138.861	1.00	12.41	0
ATOM	2222	CA	VAL	231	-2.649	55.749	137.772	1.00	9.72	0
ATOM	2223	CB	VAL	231	-2.186	56.789	136.717	1.00	2.00	0
ATOM	2224	CG1	VAL	231	-3.304	57.063	135.718	1.00	2.00	0
ATOM	2225	CG2	VAL	231	-1.728	58.077	137.396	1.00	2.00	0
ATOM	2226	C	VAL	231	-2.816	54.393	137.102	1.00	11.88	0
ATOM	2227	O	VAL	231	-3.937	53.966	136.849	1.00	2.00	0
ATOM	2228	N	VAL	232	-1.695	53.723	136.832	1.00	2.00	0
ATOM	2230	CA	VAL	232	-1.678	52.397	136.203	1.00	2.00	0
ATOM	2231	CB	VAL	232	-0.245	51.817	136.151	1.00	2.00	0
ATOM	2232	CG1	VAL	232	-0.264	50.442	135.548	1.00	2.00	0

ATOM	2233	CG2	VAL	232	0.664	52.724	135.376	1.00	2.00	0
ATOM	2234	C	VAL	232	-2.533	51.413	136.992	1.00	2.00	0
ATOM	2235	O	VAL	232	-3.449	50.787	136.454	1.00	2.00	0
ATOM	2236	N	ALA	233	-2.217	51.292	138.275	1.00	38.57	0
ATOM	2238	CA	ALA	233	-2.920	50.395	139.173	1.00	38.57	0
ATOM	2239	CB	ALA	233	-2.297	50.487	140.542	1.00	13.20	0
ATOM	2240	C	ALA	233	-4.426	50.681	139.245	1.00	38.57	0
ATOM	2241	O	ALA	233	-5.255	49.763	139.166	1.00	9.05	0
ATOM	2242	N	LYS	234	-4.780	51.954	139.397	1.00	2.00	0
ATOM	2244	CA	LYS	234	-6.177	52.355	139.477	1.00	2.00	0
ATOM	2245	CB	LYS	234	-6.270	53.843	139.803	1.00	22.96	0
ATOM	2246	CG	LYS	234	-5.776	54.160	141.205	1.00	31.42	0
ATOM	2247	CD	LYS	234	-6.667	53.499	142.257	1.00	42.09	0
ATOM	2248	CE	LYS	234	-5.916	53.151	143.543	1.00	40.07	0
ATOM	2249	NZ	LYS	234	-5.104	51.892	143.444	1.00	41.59	0
ATOM	2253	C	LYS	234	-6.920	52.036	138.183	1.00	2.00	0
ATOM	2254	O	LYS	234	-7.936	51.319	138.206	1.00	20.45	0
ATOM	2255	N	PHE	235	-6.389	52.532	137.061	1.00	14.37	0
ATOM	2257	CA	PHE	235	-6.973	52.319	135.733	1.00	14.37	0
ATOM	2258	CB	PHE	235	-6.055	52.880	134.640	1.00	2.00	0
ATOM	2259	CG	PHE	235	-6.438	52.452	133.249	1.00	2.00	0
ATOM	2260	CD1	PHE	235	-7.352	53.199	132.502	1.00	2.00	0
ATOM	2261	CD2	PHE	235	-5.924	51.270	132.706	1.00	2.00	0
ATOM	2262	CE1	PHE	235	-7.760	52.777	131.236	1.00	2.00	0
ATOM	2263	CE2	PHE	235	-6.316	50.834	131.452	1.00	2.00	0
ATOM	2264	CZ	PHE	235	-7.242	51.588	130.710	1.00	2.00	0
ATOM	2265	C	PHE	235	-7.229	50.849	135.444	1.00	14.37	0
ATOM	2266	O	PHE	235	-8.312	50.471	134.977	1.00	2.00	0
ATOM	2267	N	LEU	236	-6.217	50.029	135.690	1.00	3.08	0
ATOM	2269	CA	LEU	236	-6.339	48.606	135.447	1.00	5.72	0
ATOM	2270	CB	LEU	236	-5.018	47.900	135.731	1.00	2.00	0
ATOM	2271	CG	LEU	236	-3.915	48.136	134.710	1.00	2.00	0
ATOM	2272	CD1	LEU	236	-2.699	47.332	135.096	1.00	2.00	0
ATOM	2273	CD2	LEU	236	-4.405	47.737	133.321	1.00	2.00	0
ATOM	2274	C	LEU	236	-7.452	47.978	136.278	1.00	10.30	0
ATOM	2275	O	LEU	236	-8.389	47.398	135.712	1.00	2.00	0
ATOM	2276	N	HIS	237	-7.368	48.118	137.606	1.00	8.44	0
ATOM	2278	CA	HIS	237	-8.368	47.540	138.504	1.00	8.44	0
ATOM	2279	CB	HIS	237	-8.088	47.885	139.980	1.00	38.56	0
ATOM	2280	CG	HIS	237	-9.141	47.380	140.935	1.00	46.82	0
ATOM	2281	CD2	HIS	237	-10.323	47.916	141.329	1.00	46.01	0
ATOM	2282	ND1	HIS	237	-9.035	46.173	141.599	1.00	46.38	0
ATOM	2284	CE1	HIS	237	-10.103	45.989	142.355	1.00	50.85	0
ATOM	2285	NE2	HIS	237	-10.900	47.031	142.210	1.00	49.26	0
ATOM	2287	C	HIS	237	-9.747	48.033	138.138	1.00	8.44	0
ATOM	2288	O	HIS	237	-10.672	47.232	138.027	1.00	35.43	0
ATOM	2289	N	LYS	238	-9.882	49.346	137.947	1.00	2.00	0
ATOM	2291	CA	LYS	238	-11.183	49.923	137.607	1.00	2.00	0
ATOM	2292	CB	LYS	238	-11.071	51.424	137.327	1.00	28.00	0
ATOM	2293	CG	LYS	238	-12.427	52.103	137.104	1.00	29.80	0
ATOM	2294	CD	LYS	238	-12.322	53.628	136.829	1.00	36.02	0
ATOM	2295	CE	LYS	238	-11.917	54.444	138.083	1.00	32.99	0
ATOM	2296	NZ	LYS	238	-11.833	55.925	137.845	1.00	30.09	0
ATOM	2300	C	LYS	238	-11.776	49.215	136.403	1.00	2.00	0
ATOM	2301	O	LYS	238	-12.991	49.205	136.234	1.00	29.21	0
ATOM	2302	N	HIS	239	-10.913	48.607	135.584	1.00	2.00	0
ATOM	2304	CA	HIS	239	-11.340	47.897	134.384	1.00	2.00	0
ATOM	2305	CB	HIS	239	-10.784	48.603	133.148	1.00	2.00	0
ATOM	2306	CG	HIS	239	-11.125	50.056	133.091	1.00	2.00	0
ATOM	2307	CD2	HIS	239	-12.282	50.689	132.785	1.00	2.00	0
ATOM	2308	ND1	HIS	239	-10.217	51.046	133.397	1.00	2.00	0
ATOM	2310	CE1	HIS	239	-10.797	52.225	133.284	1.00	2.00	0
ATOM	2311	NE2	HIS	239	-12.052	52.036	132.914	1.00	2.00	0
ATOM	2313	C	HIS	239	-10.946	46.417	134.352	1.00	2.00	0
ATOM	2314	O	HIS	239	-10.938	45.798	133.295	1.00	2.00	0
ATOM	2315	N	ASP	240	-10.642	45.838	135.503	1.00	37.96	0
ATOM	2317	CA	ASP	240	-10.251	44.433	135.564	1.00	37.83	0
ATOM	2318	CB	ASP	240	-11.482	43.512	135.737	1.00	39.81	0

ATOM	2319	CG	ASP	240	-12.676	43.919	134.870	1.00	47.06	0
ATOM	2320	OD1	ASP	240	-12.687	43.571	133.666	1.00	50.73	0
ATOM	2321	OD2	ASP	240	-13.610	44.578	135.396	1.00	47.58	0
ATOM	2322	C	ASP	240	-9.393	43.985	134.385	1.00	37.76	0
ATOM	2323	O	ASP	240	-9.626	42.933	133.797	1.00	40.81	0
ATOM	2324	N	LEU	241	-8.417	44.823	134.040	1.00	2.00	0
ATOM	2326	CA	LEU	241	-7.462	44.551	132.955	1.00	2.00	0
ATOM	2327	CB	LEU	241	-7.086	45.858	132.229	1.00	2.00	0
ATOM	2328	CG	LEU	241	-8.185	46.590	131.429	1.00	2.00	0
ATOM	2329	CD1	LEU	241	-7.795	48.047	131.224	1.00	2.00	0
ATOM	2330	CD2	LEU	241	-8.435	45.899	130.087	1.00	2.00	0
ATOM	2331	C	LEU	241	-6.225	43.925	133.601	1.00	2.00	0
ATOM	2332	O	LEU	241	-6.157	43.832	134.818	1.00	2.00	0
ATOM	2333	N	ASP	242	-5.235	43.534	132.817	1.00	2.00	0
ATOM	2335	CA	ASP	242	-4.046	42.895	133.380	1.00	2.00	0
ATOM	2336	CB	ASP	242	-3.974	41.455	132.915	1.00	25.69	0
ATOM	2337	CG	ASP	242	-4.683	40.511	133.822	1.00	12.83	0
ATOM	2338	OD1	ASP	242	-5.751	40.853	134.365	1.00	16.91	0
ATOM	2339	OD2	ASP	242	-4.149	39.404	133.976	1.00	15.37	0
ATOM	2340	C	ASP	242	-2.711	43.506	133.033	1.00	2.00	0
ATOM	2341	O	ASP	242	-1.702	43.214	133.671	1.00	25.69	0
ATOM	2342	N	LEU	243	-2.689	44.317	131.994	1.00	23.97	0
ATOM	2344	CA	LEU	243	-1.440	44.899	131.539	1.00	18.84	0
ATOM	2345	CB	LEU	243	-0.644	43.799	130.822	1.00	2.00	0
ATOM	2346	CG	LEU	243	0.698	43.831	130.097	1.00	2.00	0
ATOM	2347	CD1	LEU	243	0.410	43.690	128.660	1.00	2.00	0
ATOM	2348	CD2	LEU	243	1.526	45.058	130.397	1.00	2.00	0
ATOM	2349	C	LEU	243	-1.804	46.013	130.590	1.00	19.91	0
ATOM	2350	O	LEU	243	-2.960	46.149	130.183	1.00	2.00	0
ATOM	2351	N	ILE	244	-0.834	46.849	130.283	1.00	24.04	0
ATOM	2353	CA	ILE	244	-1.070	47.919	129.354	1.00	22.40	0
ATOM	2354	CB	ILE	244	-1.164	49.269	130.067	1.00	2.00	0
ATOM	2355	CG2	ILE	244	-1.235	50.405	129.026	1.00	2.00	0
ATOM	2356	CG1	ILE	244	-2.395	49.255	130.994	1.00	2.00	0
ATOM	2357	CD1	ILE	244	-2.607	50.530	131.803	1.00	2.00	0
ATOM	2358	C	ILE	244	0.069	47.902	128.369	1.00	25.54	0
ATOM	2359	O	ILE	244	1.234	47.715	128.755	1.00	2.00	0
ATOM	2360	N	CYS	245	-0.286	48.063	127.096	1.00	2.00	0
ATOM	2362	CA	CYS	245	0.675	48.074	126.019	1.00	2.00	0
ATOM	2363	CB	CYS	245	0.403	46.930	125.077	1.00	7.03	0
ATOM	2364	SG	CYS	245	1.849	45.913	124.986	1.00	12.49	0
ATOM	2365	C	CYS	245	0.668	49.389	125.275	1.00	2.00	0
ATOM	2366	O	CYS	245	-0.362	49.842	124.782	1.00	8.03	0
ATOM	2367	N	ARG	246	1.829	50.014	125.235	1.00	2.00	0
ATOM	2369	CA	ARG	246	1.987	51.277	124.562	1.00	2.00	0
ATOM	2370	CB	ARG	246	1.763	52.438	125.541	1.00	2.00	0
ATOM	2371	CG	ARG	246	2.658	52.453	126.783	1.00	2.00	0
ATOM	2372	CD	ARG	246	3.969	53.245	126.623	1.00	2.00	0
ATOM	2373	NE	ARG	246	3.714	54.656	126.383	1.00	2.00	0
ATOM	2375	CZ	ARG	246	4.610	55.622	126.519	1.00	2.00	0
ATOM	2376	NH1	ARG	246	5.842	55.334	126.895	1.00	2.00	0
ATOM	2379	NH2	ARG	246	4.263	56.881	126.289	1.00	2.00	0
ATOM	2382	C	ARG	246	3.374	51.342	123.938	1.00	2.00	0
ATOM	2383	O	ARG	246	4.216	50.471	124.168	1.00	2.00	0
ATOM	2384	N	ALA	247	3.605	52.345	123.108	1.00	2.00	0
ATOM	2386	CA	ALA	247	4.906	52.489	122.484	1.00	2.00	0
ATOM	2387	CB	ALA	247	4.791	52.272	120.975	1.00	61.76	0
ATOM	2388	C	ALA	247	5.351	53.902	122.819	1.00	2.00	0
ATOM	2389	O	ALA	247	5.806	54.172	123.922	1.00	61.76	0
ATOM	2390	N	HIS	248	5.187	54.801	121.870	1.00	2.00	0
ATOM	2392	CA	HIS	248	5.512	56.193	122.042	1.00	2.00	0
ATOM	2393	C	HIS	248	6.959	56.579	122.361	1.00	2.00	0
ATOM	2394	O	HIS	248	7.507	57.453	121.672	1.00	2.00	0
ATOM	2395	CB	HIS	248	4.539	56.793	123.054	1.00	2.00	0
ATOM	2396	CG	HIS	248	4.255	58.246	122.837	1.00	2.00	0
ATOM	2397	ND1	HIS	248	5.262	59.147	122.594	1.00	2.00	0
ATOM	2398	CE1	HIS	248	4.677	60.327	122.535	1.00	2.00	0
ATOM	2399	CD2	HIS	248	3.074	58.906	122.913	1.00	2.00	0

ATOM	2400	NE2	HIS	248	3.359	60.234	122.721	1.00	2.00	0
ATOM	2402	N	GLN	249	7.588	55.942	123.348	1.00	7.57	0
ATOM	2404	CA	GLN	249	8.967	56.283	123.731	1.00	7.57	0
ATOM	2405	CB	GLN	249	9.010	56.722	125.192	1.00	30.82	0
ATOM	2406	CG	GLN	249	7.987	57.759	125.566	1.00	32.63	0
ATOM	2407	CD	GLN	249	8.159	58.253	126.983	1.00	33.33	0
ATOM	2408	OE1	GLN	249	7.871	59.406	127.274	1.00	39.63	0
ATOM	2409	NE2	GLN	249	8.640	57.389	127.874	1.00	32.74	0
ATOM	2412	C	GLN	249	10.052	55.222	123.529	1.00	7.57	0
ATOM	2413	O	GLN	249	9.884	54.057	123.888	1.00	28.32	0
ATOM	2414	N	VAL	250	11.185	55.664	122.988	1.00	20.32	0
ATOM	2416	CA	VAL	250	12.339	54.805	122.735	1.00	20.32	0
ATOM	2417	CB	VAL	250	13.571	55.628	122.300	1.00	6.81	0
ATOM	2418	CG1	VAL	250	14.641	54.714	121.706	1.00	6.81	0
ATOM	2419	CG2	VAL	250	13.161	56.708	121.311	1.00	6.81	0
ATOM	2420	C	VAL	250	12.733	54.034	123.998	1.00	20.32	0
ATOM	2421	O	VAL	250	12.471	54.474	125.120	1.00	6.81	0
ATOM	2422	N	VAL	251	13.372	52.887	123.797	1.00	2.00	0
ATOM	2424	CA	VAL	251	13.820	52.023	124.871	1.00	2.00	0
ATOM	2425	CB	VAL	251	12.655	51.150	125.391	1.00	9.99	0
ATOM	2426	CG1	VAL	251	11.778	51.967	126.311	1.00	9.99	0
ATOM	2427	CG2	VAL	251	11.803	50.661	124.247	1.00	9.99	0
ATOM	2428	C	VAL	251	14.960	51.167	124.316	1.00	2.00	0
ATOM	2429	O	VAL	251	14.792	50.470	123.319	1.00	9.99	0
ATOM	2430	N	GLU	252	16.118	51.224	124.972	1.00	21.55	0
ATOM	2432	CA	GLU	252	17.312	50.509	124.519	1.00	19.34	0
ATOM	2433	CB	GLU	252	18.452	50.605	125.542	1.00	11.04	0
ATOM	2434	CG	GLU	252	19.819	50.220	124.933	1.00	18.95	0
ATOM	2435	CD	GLU	252	20.926	49.966	125.962	1.00	20.82	0
ATOM	2436	OE1	GLU	252	21.938	49.303	125.597	1.00	17.37	0
ATOM	2437	OE2	GLU	252	20.782	50.422	127.126	1.00	29.06	0
ATOM	2438	C	GLU	252	17.144	49.055	124.145	1.00	19.22	0
ATOM	2439	O	GLU	252	17.838	48.571	123.261	1.00	8.64	0
ATOM	2440	N	ASP	253	16.240	48.356	124.815	1.00	2.00	0
ATOM	2442	CA	ASP	253	16.025	46.936	124.544	1.00	2.00	0
ATOM	2443	CB	ASP	253	16.125	46.144	125.850	1.00	78.16	0
ATOM	2444	CG	ASP	253	17.543	46.106	126.401	1.00	84.05	0
ATOM	2445	OD1	ASP	253	18.060	44.995	126.635	1.00	89.15	0
ATOM	2446	OD2	ASP	253	18.148	47.181	126.598	1.00	87.62	0
ATOM	2447	C	ASP	253	14.710	46.645	123.836	1.00	2.00	0
ATOM	2448	O	ASP	253	14.201	45.528	123.881	1.00	63.68	0
ATOM	2449	N	GLY	254	14.161	47.660	123.181	1.00	2.00	0
ATOM	2451	CA	GLY	254	12.919	47.483	122.457	1.00	2.00	0
ATOM	2452	C	GLY	254	11.715	47.547	123.354	1.00	2.00	0
ATOM	2453	O	GLY	254	10.694	48.124	122.993	1.00	43.70	0
ATOM	2454	N	TYR	255	11.823	46.922	124.516	1.00	2.00	0
ATOM	2456	CA	TYR	255	10.749	46.956	125.484	1.00	2.00	0
ATOM	2457	CB	TYR	255	10.047	45.614	125.571	1.00	2.00	0
ATOM	2458	CG	TYR	255	10.853	44.510	126.185	1.00	2.00	0
ATOM	2459	CD1	TYR	255	12.103	44.175	125.696	1.00	2.00	0
ATOM	2460	CE1	TYR	255	12.824	43.121	126.248	1.00	2.00	0
ATOM	2461	CD2	TYR	255	10.337	43.770	127.246	1.00	2.00	0
ATOM	2462	CE2	TYR	255	11.041	42.721	127.802	1.00	2.00	0
ATOM	2463	CZ	TYR	255	12.279	42.397	127.301	1.00	2.00	0
ATOM	2464	OH	TYR	255	12.946	41.328	127.839	1.00	2.00	0
ATOM	2466	C	TYR	255	11.262	47.375	126.847	1.00	2.00	0
ATOM	2467	O	TYR	255	12.453	47.283	127.150	1.00	2.00	0
ATOM	2468	N	GLU	256	10.336	47.853	127.656	1.00	2.00	0
ATOM	2470	CA	GLU	256	10.632	48.341	128.979	1.00	2.00	0
ATOM	2471	CB	GLU	256	11.092	49.798	128.910	1.00	20.70	0
ATOM	2472	CG	GLU	256	11.264	50.457	130.269	1.00	27.98	0
ATOM	2473	CD	GLU	256	11.485	51.961	130.179	1.00	31.28	0
ATOM	2474	OE1	GLU	256	10.726	52.725	130.834	1.00	33.21	0
ATOM	2475	OE2	GLU	256	12.418	52.378	129.453	1.00	39.87	0
ATOM	2476	C	GLU	256	9.362	48.238	129.800	1.00	2.00	0
ATOM	2477	O	GLU	256	8.299	48.743	129.420	1.00	18.74	0
ATOM	2478	N	PHE	257	9.474	47.540	130.919	1.00	2.00	0
ATOM	2480	CA	PHE	257	8.357	47.364	131.806	1.00	2.00	0

ATOM	2481	CB	PHE	257	8.578	46.139	132.661	1.00	2.00	0
ATOM	2482	CG	PHE	257	8.222	44.865	131.978	1.00	2.00	0
ATOM	2483	CD1	PHE	257	9.187	43.926	131.694	1.00	2.00	0
ATOM	2484	CD2	PHE	257	6.906	44.594	131.649	1.00	2.00	0
ATOM	2485	CE1	PHE	257	8.849	42.740	131.101	1.00	2.00	0
ATOM	2486	CE2	PHE	257	6.560	43.417	131.058	1.00	2.00	0
ATOM	2487	CZ	PHE	257	7.533	42.481	130.781	1.00	2.00	0
ATOM	2488	C	PHE	257	8.257	48.593	132.671	1.00	2.00	0
ATOM	2489	O	PHE	257	9.215	49.360	132.782	1.00	2.00	0
ATOM	2490	N	PHE	258	7.104	48.777	133.286	1.00	25.02	0
ATOM	2492	CA	PHE	258	6.884	49.916	134.147	1.00	25.02	0
ATOM	2493	CB	PHE	258	6.417	51.086	133.299	1.00	2.00	0
ATOM	2494	CG	PHE	258	5.831	52.237	134.072	1.00	2.00	0
ATOM	2495	CD1	PHE	258	6.625	53.325	134.431	1.00	2.00	0
ATOM	2496	CD2	PHE	258	4.468	52.271	134.369	1.00	2.00	0
ATOM	2497	CE1	PHE	258	6.070	54.439	135.070	1.00	2.00	0
ATOM	2498	CE2	PHE	258	3.900	53.369	135.003	1.00	2.00	0
ATOM	2499	CZ	PHE	258	4.698	54.461	135.356	1.00	2.00	0
ATOM	2500	C	PHE	258	5.837	49.508	135.160	1.00	25.02	0
ATOM	2501	O	PHE	258	4.965	48.675	134.859	1.00	2.00	0
ATOM	2502	N	ALA	259	5.953	50.063	136.368	1.00	13.61	0
ATOM	2504	CA	ALA	259	5.027	49.775	137.457	1.00	11.22	0
ATOM	2505	CB	ALA	259	3.626	50.318	137.122	1.00	2.00	0
ATOM	2506	C	ALA	259	4.951	48.286	137.729	1.00	12.73	0
ATOM	2507	O	ALA	259	3.876	47.718	137.660	1.00	2.00	0
ATOM	2508	N	LYS	260	6.091	47.657	138.016	1.00	2.00	0
ATOM	2510	CA	LYS	260	6.140	46.214	138.304	1.00	9.39	0
ATOM	2511	CB	LYS	260	5.594	45.925	139.704	1.00	20.75	0
ATOM	2512	CG	LYS	260	6.589	46.151	140.844	1.00	28.17	0
ATOM	2513	CD	LYS	260	6.797	47.622	141.177	1.00	36.91	0
ATOM	2514	CE	LYS	260	7.615	47.765	142.449	1.00	36.02	0
ATOM	2515	NZ	LYS	260	6.919	47.158	143.633	1.00	29.33	0
ATOM	2519	C	LYS	260	5.370	45.375	137.279	1.00	2.00	0
ATOM	2520	O	LYS	260	4.443	44.633	137.641	1.00	15.95	0
ATOM	2521	N	ARG	261	5.764	45.531	136.004	1.00	2.00	0
ATOM	2523	CA	ARG	261	5.173	44.843	134.851	1.00	2.00	0
ATOM	2524	CB	ARG	261	5.410	43.335	134.964	1.00	21.35	0
ATOM	2525	CG	ARG	261	6.881	42.969	134.928	1.00	21.35	0
ATOM	2526	CD	ARG	261	7.088	41.473	134.970	1.00	9.03	0
ATOM	2527	NE	ARG	261	8.408	41.097	134.460	1.00	14.18	0
ATOM	2529	CZ	ARG	261	8.801	39.842	134.222	1.00	14.38	0
ATOM	2530	NH1	ARG	261	7.976	38.820	134.462	1.00	16.12	0
ATOM	2533	NH2	ARG	261	10.018	39.603	133.729	1.00	18.11	0
ATOM	2536	C	ARG	261	3.692	45.136	134.592	1.00	2.00	0
ATOM	2537	O	ARG	261	3.009	44.343	133.933	1.00	21.35	0
ATOM	2538	N	GLN	262	3.215	46.283	135.092	1.00	7.73	0
ATOM	2540	CA	GLN	262	1.821	46.727	134.927	1.00	7.73	0
ATOM	2541	CB	GLN	262	1.379	47.620	136.100	1.00	2.00	0
ATOM	2542	CG	GLN	262	1.106	46.888	137.434	1.00	2.00	0
ATOM	2543	CD	GLN	262	0.859	47.840	138.601	1.00	2.00	0
ATOM	2544	OE1	GLN	262	-0.277	48.137	138.930	1.00	2.00	0
ATOM	2545	NE2	GLN	262	1.922	48.304	139.237	1.00	2.00	0
ATOM	2548	C	GLN	262	1.635	47.495	133.628	1.00	7.73	0
ATOM	2549	O	GLN	262	0.526	47.650	133.154	1.00	2.00	0
ATOM	2550	N	LEU	263	2.730	47.996	133.078	1.00	2.00	0
ATOM	2552	CA	LEU	263	2.723	48.726	131.819	1.00	2.00	0
ATOM	2553	CB	LEU	263	2.754	50.244	132.069	1.00	2.00	0
ATOM	2554	CG	LEU	263	3.070	51.201	130.890	1.00	2.00	0
ATOM	2555	CD1	LEU	263	2.404	52.532	131.133	1.00	2.00	0
ATOM	2556	CD2	LEU	263	4.575	51.408	130.679	1.00	2.00	0
ATOM	2557	C	LEU	263	3.991	48.305	131.089	1.00	2.00	0
ATOM	2558	O	LEU	263	5.018	48.082	131.736	1.00	2.00	0
ATOM	2559	N	VAL	264	3.932	48.207	129.759	1.00	42.92	0
ATOM	2561	CA	VAL	264	5.105	47.850	128.949	1.00	41.59	0
ATOM	2562	CB	VAL	264	5.014	46.373	128.433	1.00	2.00	0
ATOM	2563	CG1	VAL	264	3.952	46.242	127.372	1.00	2.00	0
ATOM	2564	CG2	VAL	264	6.349	45.908	127.929	1.00	2.00	0
ATOM	2565	C	VAL	264	5.193	48.840	127.772	1.00	42.79	0

ATOM	2566	O	VAL	264	4.164	49.261	127.242	1.00	2.00	0
ATOM	2567	N	THR	265	6.409	49.237	127.400	1.00	2.00	0
ATOM	2569	CA	THR	265	6.639	50.177	126.292	1.00	2.00	0
ATOM	2570	CB	THR	265	7.420	51.412	126.789	1.00	2.00	0
ATOM	2571	OG1	THR	265	6.534	52.253	127.531	1.00	2.00	0
ATOM	2573	CG2	THR	265	8.021	52.191	125.648	1.00	2.00	0
ATOM	2574	C	THR	265	7.405	49.523	125.132	1.00	2.00	0
ATOM	2575	O	THR	265	8.612	49.245	125.246	1.00	2.00	0
ATOM	2576	N	LEU	266	6.712	49.280	124.019	1.00	7.19	0
ATOM	2578	CA	LEU	266	7.330	48.653	122.857	1.00	7.19	0
ATOM	2579	CB	LEU	266	6.338	47.721	122.176	1.00	2.00	0
ATOM	2580	CG	LEU	266	5.815	46.505	122.948	1.00	2.00	0
ATOM	2581	CD1	LEU	266	4.859	45.733	122.057	1.00	2.00	0
ATOM	2582	CD2	LEU	266	6.955	45.599	123.368	1.00	2.00	0
ATOM	2583	C	LEU	266	7.898	49.618	121.819	1.00	7.19	0
ATOM	2584	O	LEU	266	7.329	50.675	121.537	1.00	2.00	0
ATOM	2585	N	PHE	267	9.033	49.249	121.247	1.00	2.00	0
ATOM	2587	CA	PHE	267	9.665	50.068	120.222	1.00	2.00	0
ATOM	2588	CB	PHE	267	10.763	50.960	120.821	1.00	2.00	0
ATOM	2589	CG	PHE	267	10.937	52.260	120.091	1.00	2.00	0
ATOM	2590	CD1	PHE	267	9.985	53.261	120.206	1.00	2.00	0
ATOM	2591	CD2	PHE	267	12.021	52.468	119.255	1.00	2.00	0
ATOM	2592	CE1	PHE	267	10.108	54.445	119.493	1.00	2.00	0
ATOM	2593	CE2	PHE	267	12.146	53.652	118.540	1.00	2.00	0
ATOM	2594	CZ	PHE	267	11.187	54.636	118.661	1.00	2.00	0
ATOM	2595	C	PHE	267	10.246	49.076	119.227	1.00	2.00	0
ATOM	2596	O	PHE	267	11.418	48.693	119.321	1.00	2.00	0
ATOM	2597	N	SER	268	9.387	48.638	118.302	1.00	12.94	0
ATOM	2599	CA	SER	268	9.707	47.648	117.267	1.00	12.94	0
ATOM	2600	CB	SER	268	8.420	47.043	116.723	1.00	11.11	0
ATOM	2601	OG	SER	268	7.593	46.579	117.771	1.00	11.11	0
ATOM	2603	C	SER	268	10.450	48.231	116.103	1.00	12.94	0
ATOM	2604	O	SER	268	10.150	49.344	115.711	1.00	11.11	0
ATOM	2605	N	ALA	269	11.391	47.454	115.556	1.00	71.01	0
ATOM	2607	CA	ALA	269	12.222	47.779	114.378	1.00	71.72	0
ATOM	2608	CB	ALA	269	11.383	48.513	113.295	1.00	82.00	0
ATOM	2609	C	ALA	269	13.585	48.469	114.543	1.00	74.82	0
ATOM	2610	O	ALA	269	14.609	47.889	114.186	1.00	91.21	0
ATOM	2611	N	PRO	270	13.619	49.704	115.076	1.00	28.82	0
ATOM	2612	CD	PRO	270	12.436	50.466	115.513	1.00	2.00	0
ATOM	2613	CA	PRO	270	14.788	50.542	115.316	1.00	31.86	0
ATOM	2614	CB	PRO	270	14.340	51.374	116.502	1.00	2.00	0
ATOM	2615	CG	PRO	270	13.034	51.783	116.023	1.00	2.00	0
ATOM	2616	C	PRO	270	16.254	50.192	115.428	1.00	29.52	0
ATOM	2617	O	PRO	270	16.716	49.072	115.272	1.00	2.00	0
ATOM	2618	N	ASN	271	16.928	51.318	115.593	1.00	2.00	0
ATOM	2620	CA	ASN	271	18.346	51.621	115.754	1.00	2.00	0
ATOM	2621	CB	ASN	271	19.168	50.935	114.663	1.00	35.96	0
ATOM	2622	CG	ASN	271	18.483	50.953	113.300	1.00	61.96	0
ATOM	2623	OD1	ASN	271	17.605	51.787	113.034	1.00	36.11	0
ATOM	2624	ND2	ASN	271	18.872	50.015	112.432	1.00	36.31	0
ATOM	2627	C	ASN	271	18.199	53.143	115.475	1.00	2.00	0
ATOM	2628	O	ASN	271	19.072	53.807	114.915	1.00	61.69	0
ATOM	2629	N	TYR	272	17.039	53.638	115.930	1.00	2.00	0
ATOM	2631	CA	TYR	272	16.489	54.978	115.793	1.00	2.00	0
ATOM	2632	CB	TYR	272	15.772	55.358	117.090	1.00	17.33	0
ATOM	2633	CG	TYR	272	14.528	56.208	116.897	1.00	10.41	0
ATOM	2634	CD1	TYR	272	13.458	55.769	116.105	1.00	11.86	0
ATOM	2635	CE1	TYR	272	12.313	56.571	115.917	1.00	14.32	0
ATOM	2636	CD2	TYR	272	14.421	57.454	117.493	1.00	10.66	0
ATOM	2637	CE2	TYR	272	13.287	58.256	117.312	1.00	15.43	0
ATOM	2638	CZ	TYR	272	12.243	57.813	116.529	1.00	9.40	0
ATOM	2639	OH	TYR	272	11.143	58.636	116.375	1.00	17.38	0
ATOM	2641	C	TYR	272	17.332	56.132	115.299	1.00	2.00	0
ATOM	2642	O	TYR	272	18.356	56.471	115.888	1.00	29.84	0
ATOM	2643	N	CYS	273	16.860	56.731	114.201	1.00	7.24	0
ATOM	2645	CA	CYS	273	17.490	57.875	113.553	1.00	6.82	0
ATOM	2646	CB	CYS	273	17.203	59.167	114.331	1.00	11.61	0

ATOM	2647	SG	CYS	273	15.496	59.459	114.843	1.00	10.42	0
ATOM	2648	C	CYS	273	19.010	57.724	113.411	1.00	8.43	0
ATOM	2649	O	CYS	273	19.738	58.717	113.512	1.00	9.04	0
ATOM	2650	N	GLY	274	19.498	56.502	113.185	1.00	13.82	0
ATOM	2652	CA	GLY	274	20.934	56.303	113.044	1.00	13.82	0
ATOM	2653	C	GLY	274	21.710	57.029	114.134	1.00	13.82	0
ATOM	2654	O	GLY	274	22.817	57.515	113.906	1.00	39.65	0
ATOM	2655	N	GLU	275	21.120	57.085	115.326	1.00	92.80	0
ATOM	2657	CA	GLU	275	21.719	57.764	116.467	1.00	91.32	0
ATOM	2658	CB	GLU	275	21.479	59.276	116.340	1.00	25.01	0
ATOM	2659	CG	GLU	275	19.994	59.656	116.224	1.00	31.82	0
ATOM	2660	CD	GLU	275	19.730	61.158	116.060	1.00	30.92	0
ATOM	2661	OE1	GLU	275	18.951	61.713	116.868	1.00	38.31	0
ATOM	2662	OE2	GLU	275	20.276	61.787	115.125	1.00	34.18	0
ATOM	2663	C	GLU	275	21.137	57.260	117.794	1.00	90.32	0
ATOM	2664	O	GLU	275	20.941	58.047	118.716	1.00	23.69	0
ATOM	2665	N	PHE	276	20.868	55.958	117.901	1.00	18.78	0
ATOM	2667	CA	PHE	276	20.303	55.412	119.134	1.00	17.07	0
ATOM	2668	CB	PHE	276	18.774	55.551	119.125	1.00	37.20	0
ATOM	2669	CG	PHE	276	18.280	56.876	119.652	1.00	35.89	0
ATOM	2670	CD1	PHE	276	17.522	57.726	118.849	1.00	35.53	0
ATOM	2671	CD2	PHE	276	18.572	57.273	120.949	1.00	39.17	0
ATOM	2672	CE1	PHE	276	17.067	58.945	119.329	1.00	31.45	0
ATOM	2673	CE2	PHE	276	18.123	58.485	121.434	1.00	36.03	0
ATOM	2674	CZ	PHE	276	17.367	59.324	120.621	1.00	39.75	0
ATOM	2675	C	PHE	276	20.681	53.992	119.597	1.00	17.79	0
ATOM	2676	O	PHE	276	20.463	53.669	120.772	1.00	38.38	0
ATOM	2677	N	ASP	277	21.213	53.140	118.712	1.00	27.69	0
ATOM	2679	CA	ASP	277	21.638	51.772	119.093	1.00	27.89	0
ATOM	2680	CB	ASP	277	22.884	51.848	120.018	1.00	0.27	0
ATOM	2681	CG	ASP	277	23.231	50.508	120.716	1.00	39.20	0
ATOM	2682	OD1	ASP	277	23.163	50.470	121.964	1.00	39.20	0
ATOM	2683	OD2	ASP	277	23.576	49.508	120.036	1.00	39.20	0
ATOM	2684	C	ASP	277	20.560	50.892	119.742	1.00	26.41	0
ATOM	2685	O	ASP	277	20.761	49.675	119.918	1.00	0.76	0
ATOM	2686	N	ASN	278	19.428	51.491	120.101	1.00	2.00	0
ATOM	2688	CA	ASN	278	18.344	50.758	120.722	1.00	2.00	0
ATOM	2689	CB	ASN	278	17.142	51.676	120.920	1.00	2.00	0
ATOM	2690	CG	ASN	278	16.394	51.930	119.639	1.00	2.00	0
ATOM	2691	OD1	ASN	278	16.867	52.643	118.765	1.00	2.00	0
ATOM	2692	ND2	ASN	278	15.225	51.324	119.510	1.00	2.00	0
ATOM	2695	C	ASN	278	17.938	49.602	119.829	1.00	2.00	0
ATOM	2696	O	ASN	278	17.970	49.710	118.600	1.00	2.00	0
ATOM	2697	N	ALA	279	17.603	48.487	120.454	1.00	14.31	0
ATOM	2699	CA	ALA	279	17.133	47.320	119.734	1.00	14.31	0
ATOM	2700	CB	ALA	279	17.281	46.081	120.594	1.00	2.00	0
ATOM	2701	C	ALA	279	15.655	47.631	119.498	1.00	14.31	0
ATOM	2702	O	ALA	279	15.155	48.645	119.996	1.00	2.00	0
ATOM	2703	N	GLY	280	14.959	46.788	118.743	1.00	2.00	0
ATOM	2705	CA	GLY	280	13.549	47.014	118.484	1.00	2.00	0
ATOM	2706	C	GLY	280	12.864	45.783	118.992	1.00	2.00	0
ATOM	2707	O	GLY	280	13.381	44.698	118.799	1.00	9.35	0
ATOM	2708	N	ALA	281	11.725	45.906	119.643	1.00	2.00	0
ATOM	2710	CA	ALA	281	11.082	44.702	120.167	1.00	2.00	0
ATOM	2711	CB	ALA	281	10.799	44.850	121.658	1.00	2.00	0
ATOM	2712	C	ALA	281	9.815	44.345	119.437	1.00	2.00	0
ATOM	2713	O	ALA	281	9.451	44.992	118.473	1.00	2.00	0
ATOM	2714	N	MET	282	9.140	43.312	119.918	1.00	14.19	0
ATOM	2716	CA	MET	282	7.907	42.833	119.315	1.00	14.19	0
ATOM	2717	CB	MET	282	8.232	42.115	117.995	1.00	25.98	0
ATOM	2718	CG	MET	282	7.056	41.885	117.060	1.00	24.91	0
ATOM	2719	SD	MET	282	7.304	40.449	115.980	1.00	25.45	0
ATOM	2720	CE	MET	282	9.044	40.644	115.525	1.00	21.20	0
ATOM	2721	C	MET	282	7.397	41.851	120.363	1.00	14.19	0
ATOM	2722	O	MET	282	8.142	40.972	120.790	1.00	24.98	0
ATOM	2723	N	MET	283	6.148	42.004	120.788	1.00	2.00	0
ATOM	2725	CA	MET	283	5.592	41.143	121.825	1.00	2.00	0
ATOM	2726	CB	MET	283	4.940	41.991	122.925	1.00	19.29	0

ATOM	2727	CG	MET	283	4.481	41.205	124.142	1.00	19.76	0
ATOM	2728	SD	MET	283	3.228	42.077	125.116	1.00	20.92	0
ATOM	2729	CE	MET	283	4.204	43.235	125.966	1.00	17.38	0
ATOM	2730	C	MET	283	4.592	40.125	121.339	1.00	2.00	0
ATOM	2731	O	MET	283	3.456	40.470	121.036	1.00	16.17	0
ATOM	2732	N	SER	284	5.012	38.871	121.291	1.00	2.00	0
ATOM	2734	CA	SER	284	4.148	37.777	120.869	1.00	2.00	0
ATOM	2735	CB	SER	284	4.991	36.664	120.220	1.00	20.90	0
ATOM	2736	OG	SER	284	6.376	36.771	120.528	1.00	23.67	0
ATOM	2738	C	SER	284	3.275	37.202	122.018	1.00	2.00	0
ATOM	2739	O	SER	284	3.777	36.595	122.978	1.00	26.24	0
ATOM	2740	N	VAL	285	1.967	37.402	121.894	1.00	2.00	0
ATOM	2742	CA	VAL	285	0.979	36.940	122.859	1.00	2.00	0
ATOM	2743	CB	VAL	285	-0.091	38.026	123.056	1.00	2.00	0
ATOM	2744	CG1	VAL	285	-0.952	37.714	124.262	1.00	2.00	0
ATOM	2745	CG2	VAL	285	0.572	39.381	123.171	1.00	2.00	0
ATOM	2746	C	VAL	285	0.274	35.644	122.417	1.00	2.00	0
ATOM	2747	O	VAL	285	-0.572	35.672	121.532	1.00	2.00	0
ATOM	2748	N	ASP	286	0.609	34.512	123.026	1.00	2.00	0
ATOM	2750	CA	ASP	286	-0.056	33.258	122.663	1.00	2.00	0
ATOM	2751	CB	ASP	286	0.771	32.019	123.071	1.00	22.05	0
ATOM	2752	CG	ASP	286	1.192	32.020	124.531	1.00	24.93	0
ATOM	2753	OD1	ASP	286	0.578	32.742	125.344	1.00	32.49	0
ATOM	2754	OD2	ASP	286	2.152	31.285	124.866	1.00	28.80	0
ATOM	2755	C	ASP	286	-1.494	33.141	123.181	1.00	2.00	0
ATOM	2756	O	ASP	286	-1.993	34.023	123.881	1.00	12.72	0
ATOM	2757	N	GLU	287	-2.144	32.036	122.817	1.00	28.94	0
ATOM	2759	CA	GLU	287	-3.543	31.744	123.153	1.00	28.07	0
ATOM	2760	CB	GLU	287	-3.912	30.340	122.657	1.00	59.96	0
ATOM	2761	CG	GLU	287	-3.610	30.049	121.177	1.00	66.13	0
ATOM	2762	CD	GLU	287	-2.139	29.730	120.890	1.00	70.85	0
ATOM	2763	OE1	GLU	287	-1.712	29.890	119.723	1.00	75.38	0
ATOM	2764	OE2	GLU	287	-1.412	29.315	121.822	1.00	73.00	0
ATOM	2765	C	GLU	287	-3.876	31.836	124.638	1.00	30.16	0
ATOM	2766	O	GLU	287	-5.017	32.074	125.029	1.00	62.37	0
ATOM	2767	N	THR	288	-2.852	31.654	125.455	1.00	41.83	0
ATOM	2769	CA	THR	288	-2.995	31.665	126.894	1.00	36.69	0
ATOM	2770	CB	THR	288	-2.269	30.449	127.457	1.00	11.26	0
ATOM	2771	OG1	THR	288	-0.865	30.552	127.171	1.00	11.65	0
ATOM	2773	CG2	THR	288	-2.827	29.171	126.800	1.00	11.00	0
ATOM	2774	C	THR	288	-2.461	32.947	127.533	1.00	36.73	0
ATOM	2775	O	THR	288	-2.015	32.948	128.675	1.00	18.83	0
ATOM	2776	N	LEU	289	-2.492	34.034	126.776	1.00	6.34	0
ATOM	2778	CA	LEU	289	-2.027	35.334	127.232	1.00	2.00	0
ATOM	2779	CB	LEU	289	-3.081	35.946	128.155	1.00	2.00	0
ATOM	2780	CG	LEU	289	-4.282	36.465	127.346	1.00	2.00	0
ATOM	2781	CD1	LEU	289	-5.390	36.973	128.263	1.00	2.00	0
ATOM	2782	CD2	LEU	289	-3.817	37.593	126.412	1.00	2.00	0
ATOM	2783	C	LEU	289	-0.615	35.454	127.826	1.00	2.00	0
ATOM	2784	O	LEU	289	-0.299	36.445	128.493	1.00	2.00	0
ATOM	2785	N	MET	290	0.244	34.475	127.566	1.00	20.85	0
ATOM	2787	CA	MET	290	1.619	34.548	128.046	1.00	23.75	0
ATOM	2788	CB	MET	290	2.238	33.156	128.212	1.00	24.81	0
ATOM	2789	CG	MET	290	3.717	33.200	128.623	1.00	23.46	0
ATOM	2790	SD	MET	290	4.726	31.867	127.935	1.00	26.75	0
ATOM	2791	CE	MET	290	5.196	32.555	126.310	1.00	29.16	0
ATOM	2792	C	MET	290	2.430	35.332	127.015	1.00	19.20	0
ATOM	2793	O	MET	290	2.545	34.910	125.858	1.00	29.26	0
ATOM	2794	N	CYS	291	3.003	36.454	127.449	1.00	2.00	0
ATOM	2796	CA	CYS	291	3.797	37.336	126.590	1.00	2.00	0
ATOM	2797	CB	CYS	291	3.624	38.773	127.062	1.00	17.87	0
ATOM	2798	SG	CYS	291	1.913	39.123	127.404	1.00	13.14	0
ATOM	2799	C	CYS	291	5.293	37.034	126.465	1.00	2.00	0
ATOM	2800	O	CYS	291	5.958	36.694	127.448	1.00	23.09	0
ATOM	2801	N	SER	292	5.808	37.187	125.244	1.00	5.71	0
ATOM	2803	CA	SER	292	7.223	36.977	124.928	1.00	9.30	0
ATOM	2804	CB	SER	292	7.385	35.709	124.098	1.00	12.57	0
ATOM	2805	OG	SER	292	6.548	34.675	124.593	1.00	20.05	0

ATOM	2807	C	SER	292	7.691	38.195	124.113	1.00	4.04	0
ATOM	2808	O	SER	292	6.867	38.867	123.485	1.00	14.24	0
ATOM	2809	N	PHE	293	8.993	38.487	124.128	1.00	2.00	0
ATOM	2811	CA	PHE	293	9.526	39.623	123.385	1.00	2.00	0
ATOM	2812	CB	PHE	293	10.077	40.676	124.337	1.00	17.01	0
ATOM	2813	CG	PHE	293	9.063	41.244	125.270	1.00	19.48	0
ATOM	2814	CD1	PHE	293	8.772	40.611	126.466	1.00	23.05	0
ATOM	2815	CD2	PHE	293	8.414	42.426	124.967	1.00	21.44	0
ATOM	2816	CE1	PHE	293	7.852	41.146	127.352	1.00	24.82	0
ATOM	2817	CE2	PHE	293	7.494	42.968	125.845	1.00	20.24	0
ATOM	2818	CZ	PHE	293	7.213	42.325	127.044	1.00	22.28	0
ATOM	2819	C	PHE	293	10.641	39.259	122.412	1.00	2.00	0
ATOM	2820	O	PHE	293	11.715	38.839	122.853	1.00	17.14	0
ATOM	2821	N	GLN	294	10.390	39.418	121.104	1.00	2.00	0
ATOM	2823	CA	GLN	294	11.404	39.162	120.060	1.00	2.00	0
ATOM	2824	CB	GLN	294	10.748	38.742	118.743	1.00	14.58	0
ATOM	2825	CG	GLN	294	10.074	37.383	118.798	1.00	22.67	0
ATOM	2826	CD	GLN	294	8.684	37.387	118.179	1.00	24.62	0
ATOM	2827	OE1	GLN	294	7.835	38.206	118.535	1.00	27.17	0
ATOM	2828	NE2	GLN	294	8.441	36.456	117.258	1.00	25.84	0
ATOM	2831	C	GLN	294	12.182	40.464	119.855	1.00	2.00	0
ATOM	2832	O	GLN	294	11.587	41.528	119.660	1.00	20.63	0
ATOM	2833	N	ILE	295	13.507	40.379	119.893	1.00	11.23	0
ATOM	2835	CA	ILE	295	14.356	41.569	119.772	1.00	12.32	0
ATOM	2836	CB	ILE	295	15.400	41.624	120.968	1.00	10.45	0
ATOM	2837	CG2	ILE	295	16.277	42.875	120.886	1.00	10.45	0
ATOM	2838	CG1	ILE	295	14.674	41.607	122.324	1.00	10.45	0
ATOM	2839	CD1	ILE	295	13.756	42.807	122.580	1.00	10.45	0
ATOM	2840	C	ILE	295	15.126	41.703	118.453	1.00	7.79	0
ATOM	2841	O	ILE	295	15.723	40.741	117.974	1.00	10.45	0
ATOM	2842	N	LEU	296	15.087	42.900	117.873	1.00	11.71	0
ATOM	2844	CA	LEU	296	15.824	43.235	116.658	1.00	13.33	0
ATOM	2845	CB	LEU	296	14.987	44.102	115.717	1.00	24.46	0
ATOM	2846	CG	LEU	296	13.835	43.467	114.946	1.00	22.89	0
ATOM	2847	CD1	LEU	296	12.626	43.340	115.862	1.00	22.12	0
ATOM	2848	CD2	LEU	296	13.499	44.331	113.732	1.00	19.71	0
ATOM	2849	C	LEU	296	16.965	44.070	117.224	1.00	13.82	0
ATOM	2850	O	LEU	296	16.785	45.260	117.485	1.00	13.73	0
ATOM	2851	N	LYS	297	18.135	43.454	117.381	1.00	2.00	0
ATOM	2853	CA	LYS	297	19.319	44.087	117.997	1.00	2.00	0
ATOM	2854	CB	LYS	297	20.224	42.971	118.527	1.00	79.20	0
ATOM	2855	CG	LYS	297	20.792	42.094	117.419	1.00	79.65	0
ATOM	2856	CD	LYS	297	21.898	41.187	117.915	1.00	76.76	0
ATOM	2857	CE	LYS	297	22.543	40.430	116.762	1.00	71.01	0
ATOM	2858	NZ	LYS	297	23.644	39.543	117.232	1.00	68.76	0
ATOM	2862	C	LYS	297	20.259	45.149	117.376	1.00	2.00	0
ATOM	2863	O	LYS	297	21.255	45.501	118.013	1.00	94.11	0
ATOM	2864	N	PRO	298	19.995	45.656	116.152	1.00	40.11	0
ATOM	2865	CD	PRO	298	18.942	45.297	115.188	1.00	2.00	0
ATOM	2866	CA	PRO	298	20.900	46.658	115.553	1.00	40.11	0
ATOM	2867	CB	PRO	298	20.220	46.981	114.227	1.00	2.00	0
ATOM	2868	CG	PRO	298	19.570	45.700	113.886	1.00	2.00	0
ATOM	2869	C	PRO	298	21.264	47.935	116.312	1.00	40.11	0
ATOM	2870	O	PRO	298	21.041	48.056	117.514	1.00	2.00	0
ATOM	2871	N	ALA	299	21.854	48.878	115.574	1.00	61.74	0
ATOM	2873	CA	ALA	299	22.276	50.176	116.101	1.00	61.74	0
ATOM	2874	CB	ALA	299	23.627	50.063	116.799	1.00	2.00	0
ATOM	2875	C	ALA	299	22.373	51.193	114.973	1.00	61.74	0
ATOM	2876	O	ALA	299	21.893	52.319	115.105	1.00	2.00	0
ATOM	2877	N	ASN	508	41.191	29.848	91.500	1.00	48.97	0
ATOM	2879	CA	ASN	508	39.902	30.150	90.896	1.00	48.97	0
ATOM	2880	CB	ASN	508	38.951	30.831	91.887	1.00	0.74	0
ATOM	2881	CG	ASN	508	37.666	31.359	91.203	1.00	0.74	0
ATOM	2882	OD1	ASN	508	36.879	30.587	90.592	1.00	0.74	0
ATOM	2883	ND2	ASN	508	37.453	32.682	91.290	1.00	0.74	0
ATOM	2886	C	ASN	508	40.096	31.041	89.687	1.00	48.97	0
ATOM	2887	O	ASN	508	40.274	32.266	89.798	1.00	0.74	0
ATOM	2888	N	ILE	509	40.006	30.387	88.533	1.00	17.27	0

ATOM	2890	CA	ILE	509	40.188	30.983	87.224	1.00	18.75	0
ATOM	2891	CB	ILE	509	40.088	29.889	86.127	1.00	44.37	0
ATOM	2892	CG2	ILE	509	38.650	29.700	85.673	1.00	52.59	0
ATOM	2893	CG1	ILE	509	41.013	30.238	84.966	1.00	44.31	0
ATOM	2894	CD1	ILE	509	42.489	30.093	85.305	1.00	44.07	0
ATOM	2895	C	ILE	509	39.196	32.089	86.957	1.00	18.83	0
ATOM	2896	O	ILE	509	39.463	32.956	86.131	1.00	44.94	0
ATOM	2897	N	ASP	510	38.070	32.071	87.670	1.00	2.00	0
ATOM	2899	CA	ASP	510	37.048	33.088	87.485	1.00	2.00	0
ATOM	2900	CB	ASP	510	35.711	32.605	88.031	1.00	52.76	0
ATOM	2901	CG	ASP	510	35.029	31.634	87.089	1.00	54.58	0
ATOM	2902	OD1	ASP	510	34.008	32.015	86.483	1.00	54.54	0
ATOM	2903	OD2	ASP	510	35.521	30.497	86.944	1.00	58.16	0
ATOM	2904	C	ASP	510	37.403	34.442	88.056	1.00	2.00	0
ATOM	2905	O	ASP	510	37.016	35.464	87.490	1.00	52.34	0
ATOM	2906	N	SER	511	38.143	34.471	89.160	1.00	2.00	0
ATOM	2908	CA	SER	511	38.548	35.763	89.739	1.00	2.00	0
ATOM	2909	CB	SER	511	39.372	35.570	91.015	1.00	53.95	0
ATOM	2910	OG	SER	511	38.631	34.907	92.020	1.00	50.17	0
ATOM	2912	C	SER	511	39.447	36.379	88.690	1.00	2.00	0
ATOM	2913	O	SER	511	39.228	37.488	88.203	1.00	59.62	0
ATOM	2914	N	ILE	512	40.453	35.584	88.349	1.00	45.56	0
ATOM	2916	CA	ILE	512	41.462	35.892	87.361	1.00	40.32	0
ATOM	2917	CB	ILE	512	42.224	34.598	87.035	1.00	2.00	0
ATOM	2918	CG2	ILE	512	43.250	34.842	85.943	1.00	2.00	0
ATOM	2919	CG1	ILE	512	42.897	34.092	88.316	1.00	2.00	0
ATOM	2920	CD1	ILE	512	43.635	32.772	88.174	1.00	2.00	0
ATOM	2921	C	ILE	512	40.843	36.514	86.105	1.00	41.22	0
ATOM	2922	O	ILE	512	41.051	37.700	85.848	1.00	2.00	0
ATOM	2923	N	ILE	513	40.061	35.728	85.358	1.00	2.00	0
ATOM	2925	CA	ILE	513	39.408	36.195	84.136	1.00	2.00	0
ATOM	2926	CB	ILE	513	38.435	35.123	83.529	1.00	2.00	0
ATOM	2927	CG2	ILE	513	37.560	35.757	82.455	1.00	2.00	0
ATOM	2928	CG1	ILE	513	39.227	33.963	82.890	1.00	2.00	0
ATOM	2929	CD1	ILE	513	38.365	32.796	82.367	1.00	2.00	0
ATOM	2930	C	ILE	513	38.640	37.493	84.335	1.00	2.00	0
ATOM	2931	O	ILE	513	38.764	38.403	83.519	1.00	2.00	0
ATOM	2932	N	GLN	514	37.858	37.611	85.402	1.00	12.46	0
ATOM	2934	CA	GLN	514	37.117	38.853	85.581	1.00	12.46	0
ATOM	2935	CB	GLN	514	35.985	38.678	86.591	1.00	26.62	0
ATOM	2936	CG	GLN	514	36.384	38.251	87.972	1.00	26.62	0
ATOM	2937	CD	GLN	514	35.195	38.279	88.929	1.00	26.62	0
ATOM	2938	OE1	GLN	514	34.582	39.337	89.140	1.00	26.62	0
ATOM	2939	NE2	GLN	514	34.851	37.116	89.502	1.00	26.62	0
ATOM	2942	C	GLN	514	38.009	40.055	85.936	1.00	12.46	0
ATOM	2943	O	GLN	514	37.686	41.205	85.613	1.00	26.62	0
ATOM	2944	N	ARG	515	39.147	39.773	86.564	1.00	6.50	0
ATOM	2946	CA	ARG	515	40.090	40.810	86.937	1.00	7.53	0
ATOM	2947	CB	ARG	515	41.125	40.251	87.917	1.00	8.04	0
ATOM	2948	CG	ARG	515	40.626	40.257	89.362	1.00	8.04	0
ATOM	2949	CD	ARG	515	41.182	39.117	90.212	1.00	8.04	0
ATOM	2950	NE	ARG	515	42.609	39.250	90.490	1.00	8.04	0
ATOM	2952	CZ	ARG	515	43.355	38.276	90.998	1.00	8.04	0
ATOM	2953	NH1	ARG	515	42.805	37.103	91.275	1.00	8.04	0
ATOM	2956	NH2	ARG	515	44.646	38.478	91.228	1.00	8.04	0
ATOM	2959	C	ARG	515	40.745	41.325	85.669	1.00	12.92	0
ATOM	2960	O	ARG	515	40.840	42.537	85.464	1.00	8.04	0
ATOM	2961	N	LEU	516	41.167	40.398	84.810	1.00	8.93	0
ATOM	2963	CA	LEU	516	41.788	40.727	83.525	1.00	6.71	0
ATOM	2964	CB	LEU	516	42.172	39.431	82.786	1.00	2.00	0
ATOM	2965	CG	LEU	516	43.298	38.561	83.385	1.00	2.00	0
ATOM	2966	CD1	LEU	516	43.057	37.096	83.083	1.00	2.00	0
ATOM	2967	CD2	LEU	516	44.650	38.986	82.843	1.00	2.00	0
ATOM	2968	C	LEU	516	40.809	41.562	82.675	1.00	5.82	0
ATOM	2969	O	LEU	516	41.187	42.516	82.002	1.00	2.00	0
ATOM	2970	N	LEU	517	39.534	41.228	82.755	1.00	2.00	0
ATOM	2972	CA	LEU	517	38.519	41.928	81.993	1.00	2.73	0
ATOM	2973	CB	LEU	517	37.336	40.993	81.752	1.00	7.08	0

ATOM	2974	CG	LEU	517	37.203	40.297	80.398	1.00	3.18	0
ATOM	2975	CD1	LEU	517	38.524	39.694	79.950	1.00	12.86	0
ATOM	2976	CD2	LEU	517	36.133	39.227	80.518	1.00	9.89	0
ATOM	2977	C	LEU	517	37.989	43.262	82.536	1.00	9.79	0
ATOM	2978	O	LEU	517	37.169	43.908	81.858	1.00	16.46	0
ATOM	2979	N	GLU	518	38.409	43.708	83.722	1.00	2.00	0
ATOM	2981	CA	GLU	518	37.845	44.981	84.178	1.00	2.00	0
ATOM	2982	CB	GLU	518	37.621	45.015	85.699	1.00	2.00	0
ATOM	2983	CG	GLU	518	36.908	46.315	86.231	1.00	2.00	0
ATOM	2984	CD	GLU	518	35.550	46.705	85.526	1.00	2.00	0
ATOM	2985	OE1	GLU	518	34.554	47.001	86.262	1.00	2.00	0
ATOM	2986	OE2	GLU	518	35.481	46.748	84.252	1.00	2.00	0
ATOM	2987	C	GLU	518	38.618	46.200	83.677	1.00	2.00	0
ATOM	2988	O	GLU	518	38.121	47.335	83.729	1.00	2.00	0
ATOM	2989	N	VAL	519	39.828	45.978	83.166	1.00	21.94	0
ATOM	2991	CA	VAL	519	40.582	47.094	82.589	1.00	19.66	0
ATOM	2992	CB	VAL	519	42.078	46.804	82.428	1.00	40.73	0
ATOM	2993	CG1	VAL	519	42.759	46.806	83.771	1.00	42.53	0
ATOM	2994	CG2	VAL	519	42.272	45.488	81.684	1.00	37.62	0
ATOM	2995	C	VAL	519	40.007	47.307	81.196	1.00	22.58	0
ATOM	2996	O	VAL	519	40.402	48.229	80.493	1.00	48.07	0
ATOM	2997	N	ARG	520	39.066	46.442	80.815	1.00	26.87	0
ATOM	2999	CA	ARG	520	38.410	46.495	79.515	1.00	28.58	0
ATOM	3000	CB	ARG	520	37.216	45.534	79.480	1.00	40.18	0
ATOM	3001	CG	ARG	520	36.878	45.043	78.086	1.00	44.14	0
ATOM	3002	CD	ARG	520	35.994	43.814	78.116	1.00	47.95	0
ATOM	3003	NE	ARG	520	34.592	44.131	77.872	1.00	44.40	0
ATOM	3005	CZ	ARG	520	33.565	43.402	78.308	1.00	51.11	0
ATOM	3006	NH1	ARG	520	33.767	42.298	79.022	1.00	48.24	0
ATOM	3009	NH2	ARG	520	32.325	43.778	78.026	1.00	49.03	0
ATOM	3012	C	ARG	520	37.946	47.899	79.147	1.00	28.36	0
ATOM	3013	O	ARG	520	37.881	48.247	77.964	1.00	46.63	0
ATOM	3014	N	GLY	521	37.639	48.703	80.158	1.00	27.79	0
ATOM	3016	CA	GLY	521	37.186	50.056	79.905	1.00	30.97	0
ATOM	3017	C	GLY	521	38.158	51.099	80.400	1.00	32.39	0
ATOM	3018	O	GLY	521	37.739	52.124	80.940	1.00	54.55	0
ATOM	3019	N	SER	522	39.451	50.840	80.225	1.00	46.95	0
ATOM	3021	CA	SER	522	40.495	51.761	80.663	1.00	47.91	0
ATOM	3022	CB	SER	522	41.300	51.146	81.801	1.00	33.41	0
ATOM	3023	OG	SER	522	40.459	50.694	82.844	1.00	32.38	0
ATOM	3025	C	SER	522	41.436	52.094	79.517	1.00	49.38	0
ATOM	3026	O	SER	522	41.495	51.378	78.513	1.00	34.02	0
ATOM	3027	N	LYS	523	42.174	53.184	79.679	1.00	84.47	0
ATOM	3029	CA	LYS	523	43.127	53.640	78.674	1.00	81.24	0
ATOM	3030	CB	LYS	523	44.035	54.715	79.274	1.00	43.78	0
ATOM	3031	CG	LYS	523	43.307	55.987	79.619	1.00	44.40	0
ATOM	3032	CD	LYS	523	44.206	56.990	80.322	1.00	68.84	0
ATOM	3033	CE	LYS	523	43.493	58.336	80.458	1.00	44.38	0
ATOM	3034	NZ	LYS	523	42.092	58.186	80.983	1.00	44.06	0
ATOM	3038	C	LYS	523	44.000	52.501	78.173	1.00	80.03	0
ATOM	3039	O	LYS	523	44.314	51.584	78.937	1.00	43.77	0
ATOM	3040	N	PRO	524	44.360	52.514	76.873	1.00	2.00	0
ATOM	3041	CD	PRO	524	43.901	53.427	75.811	1.00	84.06	0
ATOM	3042	CA	PRO	524	45.218	51.459	76.316	1.00	2.00	0
ATOM	3043	CB	PRO	524	45.357	51.871	74.850	1.00	82.26	0
ATOM	3044	CG	PRO	524	44.057	52.574	74.576	1.00	78.74	0
ATOM	3045	C	PRO	524	46.576	51.489	77.063	1.00	2.00	0
ATOM	3046	O	PRO	524	47.510	52.190	76.653	1.00	76.15	0
ATOM	3047	N	GLY	525	46.647	50.742	78.166	1.00	33.80	0
ATOM	3049	CA	GLY	525	47.846	50.682	78.984	1.00	98.68	0
ATOM	3050	C	GLY	525	47.575	50.197	80.403	1.00	99.00	0
ATOM	3051	O	GLY	525	48.427	49.555	81.013	1.00	2.00	0
ATOM	3052	N	LYS	526	46.397	50.496	80.942	1.00	49.37	0
ATOM	3054	CA	LYS	526	46.047	50.070	82.297	1.00	44.35	0
ATOM	3055	CB	LYS	526	44.537	50.226	82.505	1.00	0.79	0
ATOM	3056	CG	LYS	526	44.013	49.851	83.911	1.00	0.82	0
ATOM	3057	CD	LYS	526	44.370	50.915	84.950	1.00	0.29	0
ATOM	3058	CE	LYS	526	44.413	50.312	86.354	1.00	28.48	0

ATOM	3059	NZ	LYS	526	45.166	51.143	87.348	1.00	28.16	0
ATOM	3063	C	LYS	526	46.461	48.602	82.479	1.00	41.81	0
ATOM	3064	O	LYS	526	45.984	47.727	81.760	1.00	0.75	0
ATOM	3065	N	ASN	527	47.372	48.337	83.412	1.00	6.60	0
ATOM	3067	CA	ASN	527	47.861	46.972	83.639	1.00	6.60	0
ATOM	3068	CB	ASN	527	49.208	46.977	84.381	1.00	20.38	0
ATOM	3069	CG	ASN	527	50.300	47.733	83.645	1.00	30.42	0
ATOM	3070	OD1	ASN	527	50.695	48.820	84.068	1.00	29.99	0
ATOM	3071	ND2	ASN	527	50.818	47.148	82.561	1.00	30.17	0
ATOM	3074	C	ASN	527	46.895	46.135	84.463	1.00	6.60	0
ATOM	3075	O	ASN	527	45.866	46.628	84.924	1.00	23.47	0
ATOM	3076	N	VAL	528	47.271	44.866	84.647	1.00	26.67	0
ATOM	3078	CA	VAL	528	46.541	43.874	85.443	1.00	26.67	0
ATOM	3079	CB	VAL	528	45.575	43.004	84.603	1.00	33.44	0
ATOM	3080	CG1	VAL	528	44.909	41.956	85.488	1.00	33.01	0
ATOM	3081	CG2	VAL	528	44.524	43.858	83.956	1.00	35.61	0
ATOM	3082	C	VAL	528	47.607	42.940	86.018	1.00	26.67	0
ATOM	3083	O	VAL	528	48.054	42.003	85.348	1.00	36.85	0
ATOM	3084	N	GLN	529	48.048	43.231	87.239	1.00	2.00	0
ATOM	3086	CA	GLN	529	49.061	42.407	87.920	1.00	2.00	0
ATOM	3087	CB	GLN	529	49.968	43.297	88.787	1.00	30.41	0
ATOM	3088	CG	GLN	529	51.142	42.569	89.428	1.00	32.34	0
ATOM	3089	CD	GLN	529	52.380	42.558	88.558	1.00	31.37	0
ATOM	3090	OE1	GLN	529	53.436	43.035	88.962	1.00	35.47	0
ATOM	3091	NE2	GLN	529	52.259	42.014	87.361	1.00	30.69	0
ATOM	3094	C	GLN	529	48.350	41.347	88.792	1.00	2.00	0
ATOM	3095	O	GLN	529	47.545	41.689	89.663	1.00	32.29	0
ATOM	3096	N	LEU	530	48.624	40.072	88.536	1.00	2.00	0
ATOM	3098	CA	LEU	530	47.994	39.002	89.303	1.00	2.00	0
ATOM	3099	CB	LEU	530	47.462	37.911	88.381	1.00	12.99	0
ATOM	3100	CG	LEU	530	46.535	38.302	87.248	1.00	12.99	0
ATOM	3101	CD1	LEU	530	47.297	38.159	85.956	1.00	12.99	0
ATOM	3102	CD2	LEU	530	45.313	37.403	87.243	1.00	12.99	0
ATOM	3103	C	LEU	530	49.002	38.365	90.236	1.00	2.00	0
ATOM	3104	O	LEU	530	50.207	38.543	90.067	1.00	12.99	0
ATOM	3105	N	GLN	531	48.516	37.622	91.221	1.00	2.00	0
ATOM	3107	CA	GLN	531	49.418	36.932	92.117	1.00	2.00	0
ATOM	3108	CB	GLN	531	48.634	36.051	93.090	1.00	61.54	0
ATOM	3109	CG	GLN	531	48.376	36.639	94.465	1.00	62.91	0
ATOM	3110	CD	GLN	531	47.221	37.603	94.487	1.00	63.71	0
ATOM	3111	OE1	GLN	531	47.322	38.684	95.053	1.00	59.60	0
ATOM	3112	NE2	GLN	531	46.111	37.219	93.876	1.00	61.96	0
ATOM	3115	C	GLN	531	50.337	36.040	91.266	1.00	2.00	0
ATOM	3116	O	GLN	531	49.859	35.276	90.422	1.00	67.15	0
ATOM	3117	N	GLU	532	51.647	36.153	91.480	1.00	2.00	0
ATOM	3119	CA	GLU	532	52.655	35.349	90.766	1.00	2.00	0
ATOM	3120	CB	GLU	532	54.056	35.623	91.336	1.00	19.01	0
ATOM	3121	CG	GLU	532	55.176	34.623	90.966	1.00	22.74	0
ATOM	3122	CD	GLU	532	56.496	34.871	91.746	1.00	25.50	0
ATOM	3123	OE1	GLU	532	56.845	36.042	92.058	1.00	20.16	0
ATOM	3124	OE2	GLU	532	57.195	33.879	92.051	1.00	20.82	0
ATOM	3125	C	GLU	532	52.345	33.866	90.900	1.00	2.00	0
ATOM	3126	O	GLU	532	52.833	33.059	90.116	1.00	17.28	0
ATOM	3127	N	ASN	533	51.568	33.509	91.918	1.00	26.78	0
ATOM	3129	CA	ASN	533	51.181	32.120	92.127	1.00	27.69	0
ATOM	3130	CB	ASN	533	50.751	31.857	93.587	1.00	42.65	0
ATOM	3131	CG	ASN	533	49.834	32.944	94.154	1.00	49.17	0
ATOM	3132	OD1	ASN	533	50.274	34.070	94.392	1.00	50.06	0
ATOM	3133	ND2	ASN	533	48.568	32.605	94.387	1.00	50.92	0
ATOM	3136	C	ASN	533	50.053	31.770	91.165	1.00	26.24	0
ATOM	3137	O	ASN	533	49.918	30.615	90.747	1.00	41.80	0
ATOM	3138	N	GLU	534	49.253	32.777	90.815	1.00	24.76	0
ATOM	3140	CA	GLU	534	48.146	32.592	89.893	1.00	19.83	0
ATOM	3141	CB	GLU	534	47.228	33.801	89.918	1.00	17.15	0
ATOM	3142	CG	GLU	534	46.509	33.924	91.239	1.00	23.75	0
ATOM	3143	CD	GLU	534	45.598	35.132	91.323	1.00	25.22	0
ATOM	3144	OE1	GLU	534	44.490	34.997	91.890	1.00	24.06	0
ATOM	3145	OE2	GLU	534	45.991	36.215	90.837	1.00	29.17	0

ATOM	3146	C	GLU	534	48.712	32.365	88.510	1.00	21.16	0
ATOM	3147	O	GLU	534	48.235	31.500	87.779	1.00	14.12	0
ATOM	3148	N	ILE	535	49.747	33.122	88.156	1.00	2.00	0
ATOM	3150	CA	ILE	535	50.389	32.942	86.859	1.00	2.00	0
ATOM	3151	CB	ILE	535	51.442	34.023	86.570	1.00	2.00	0
ATOM	3152	CG2	ILE	535	52.050	33.784	85.190	1.00	2.00	0
ATOM	3153	CG1	ILE	535	50.793	35.411	86.641	1.00	2.00	0
ATOM	3154	CD1	ILE	535	51.537	36.488	85.849	1.00	2.00	0
ATOM	3155	C	ILE	535	51.060	31.565	86.797	1.00	2.00	0
ATOM	3156	O	ILE	535	50.788	30.780	85.876	1.00	2.00	0
ATOM	3157	N	ARG	536	51.914	31.256	87.778	1.00	2.00	0
ATOM	3159	CA	ARG	536	52.583	29.951	87.793	1.00	2.00	0
ATOM	3160	CB	ARG	536	53.495	29.818	89.011	1.00	39.13	0
ATOM	3161	CG	ARG	536	52.808	29.604	90.341	1.00	45.43	0
ATOM	3162	CD	ARG	536	53.839	29.648	91.474	1.00	49.26	0
ATOM	3163	NE	ARG	536	55.059	28.910	91.132	1.00	56.04	0
ATOM	3165	CZ	ARG	536	55.110	27.603	90.876	1.00	55.24	0
ATOM	3166	NH1	ARG	536	54.011	26.860	90.920	1.00	53.92	0
ATOM	3169	NH2	ARG	536	56.267	27.032	90.576	1.00	44.45	0
ATOM	3172	C	ARG	536	51.562	28.811	87.742	1.00	2.00	0
ATOM	3173	O	ARG	536	51.806	27.778	87.126	1.00	37.01	0
ATOM	3174	N	GLY	537	50.406	29.033	88.363	1.00	2.00	0
ATOM	3176	CA	GLY	537	49.345	28.046	88.340	1.00	2.00	0
ATOM	3177	C	GLY	537	48.690	28.000	86.970	1.00	2.00	0
ATOM	3178	O	GLY	537	48.292	26.924	86.512	1.00	2.00	0
ATOM	3179	N	LEU	538	48.574	29.164	86.319	1.00	9.51	0
ATOM	3181	CA	LEU	538	47.979	29.276	84.977	1.00	7.63	0
ATOM	3182	CB	LEU	538	47.930	30.736	84.513	1.00	2.00	0
ATOM	3183	CG	LEU	538	46.654	31.524	84.772	1.00	2.00	0
ATOM	3184	CD1	LEU	538	46.865	32.966	84.408	1.00	2.00	0
ATOM	3185	CD2	LEU	538	45.531	30.940	83.972	1.00	2.00	0
ATOM	3186	C	LEU	538	48.816	28.472	84.000	1.00	12.73	0
ATOM	3187	O	LEU	538	48.295	27.635	83.271	1.00	2.00	0
ATOM	3188	N	CYS	539	50.120	28.724	84.000	1.00	2.00	0
ATOM	3190	CA	CYS	539	51.036	28.001	83.132	1.00	2.00	0
ATOM	3191	CB	CYS	539	52.473	28.494	83.337	1.00	20.52	0
ATOM	3192	SG	CYS	539	52.713	30.280	83.567	1.00	19.48	0
ATOM	3193	C	CYS	539	50.957	26.501	83.474	1.00	2.00	0
ATOM	3194	O	CYS	539	50.854	25.658	82.588	1.00	29.69	0
ATOM	3195	N	LEU	540	50.984	26.191	84.769	1.00	26.60	0
ATOM	3197	CA	LEU	540	50.919	24.819	85.265	1.00	26.60	0
ATOM	3198	CB	LEU	540	51.106	24.818	86.786	1.00	2.00	0
ATOM	3199	CG	LEU	540	52.539	24.770	87.339	1.00	2.00	0
ATOM	3200	CD1	LEU	540	53.001	23.360	87.385	1.00	2.00	0
ATOM	3201	CD2	LEU	540	53.492	25.577	86.497	1.00	2.00	0
ATOM	3202	C	LEU	540	49.635	24.061	84.899	1.00	26.60	0
ATOM	3203	O	LEU	540	49.677	22.856	84.619	1.00	2.00	0
ATOM	3204	N	LYS	541	48.500	24.756	84.901	1.00	13.81	0
ATOM	3206	CA	LYS	541	47.219	24.126	84.561	1.00	17.46	0
ATOM	3207	CB	LYS	541	46.046	24.964	85.108	1.00	14.61	0
ATOM	3208	CG	LYS	541	45.844	24.880	86.624	1.00	22.53	0
ATOM	3209	CD	LYS	541	44.709	25.777	87.150	1.00	31.64	0
ATOM	3210	CE	LYS	541	45.175	27.201	87.517	1.00	37.15	0
ATOM	3211	NZ	LYS	541	44.147	28.010	88.284	1.00	27.95	0
ATOM	3215	C	LYS	541	47.047	23.891	83.046	1.00	16.97	0
ATOM	3216	O	LYS	541	46.862	22.745	82.608	1.00	8.92	0
ATOM	3217	N	SER	542	47.131	24.963	82.253	1.00	2.00	0
ATOM	3219	CA	SER	542	46.975	24.877	80.791	1.00	2.00	0
ATOM	3220	CB	SER	542	47.165	26.256	80.150	1.00	2.00	0
ATOM	3221	OG	SER	542	48.499	26.703	80.298	1.00	2.00	0
ATOM	3223	C	SER	542	47.915	23.870	80.107	1.00	2.00	0
ATOM	3224	O	SER	542	47.450	22.991	79.377	1.00	2.00	0
ATOM	3225	N	ARG	543	49.223	24.016	80.338	1.00	8.64	0
ATOM	3227	CA	ARG	543	50.244	23.128	79.772	1.00	8.64	0
ATOM	3228	CB	ARG	543	51.607	23.381	80.434	1.00	2.00	0
ATOM	3229	CG	ARG	543	52.676	22.339	80.116	1.00	4.46	0
ATOM	3230	CD	ARG	543	53.757	22.313	81.173	1.00	2.00	0
ATOM	3231	NE	ARG	543	54.989	21.663	80.708	1.00	2.00	0

ATOM	3233	CZ	ARG	543	55.326	20.395	80.952	1.00	2.00	0
ATOM	3234	NH1	ARG	543	54.523	19.606	81.656	1.00	3.99	0
ATOM	3237	NH2	ARG	543	56.483	19.915	80.508	1.00	2.00	0
ATOM	3240	C	ARG	543	49.873	21.660	79.981	1.00	8.64	0
ATOM	3241	O	ARG	543	50.187	20.806	79.148	1.00	5.52	0
ATOM	3242	N	GLU	544	49.227	21.352	81.098	1.00	42.94	0
ATOM	3244	CA	GLU	544	48.834	19.978	81.355	1.00	44.22	0
ATOM	3245	CB	GLU	544	48.308	19.841	82.778	1.00	37.01	0
ATOM	3246	CG	GLU	544	48.175	18.415	83.249	1.00	41.48	0
ATOM	3247	CD	GLU	544	47.561	18.341	84.626	1.00	46.37	0
ATOM	3248	OE1	GLU	544	46.433	18.858	84.791	1.00	53.09	0
ATOM	3249	OE2	GLU	544	48.202	17.777	85.543	1.00	47.19	0
ATOM	3250	C	GLU	544	47.763	19.584	80.339	1.00	40.49	0
ATOM	3251	O	GLU	544	47.742	18.450	79.867	1.00	34.80	0
ATOM	3252	N	ILE	545	46.898	20.538	79.994	1.00	2.00	0
ATOM	3254	CA	ILE	545	45.823	20.315	79.017	1.00	2.00	0
ATOM	3255	CB	ILE	545	44.805	21.487	78.959	1.00	11.87	0
ATOM	3256	CG2	ILE	545	43.645	21.102	78.064	1.00	6.53	0
ATOM	3257	CG1	ILE	545	44.288	21.836	80.353	1.00	16.65	0
ATOM	3258	CD1	ILE	545	43.267	22.955	80.361	1.00	13.01	0
ATOM	3259	C	ILE	545	46.377	20.149	77.605	1.00	2.00	0
ATOM	3260	O	ILE	545	45.960	19.267	76.868	1.00	9.05	0
ATOM	3261	N	PHE	546	47.302	21.018	77.227	1.00	2.00	0
ATOM	3263	CA	PHE	546	47.895	20.945	75.918	1.00	2.00	0
ATOM	3264	CB	PHE	546	49.058	21.906	75.816	1.00	2.00	0
ATOM	3265	CG	PHE	546	48.653	23.335	75.875	1.00	2.00	0
ATOM	3266	CD1	PHE	546	49.512	24.293	76.399	1.00	2.00	0
ATOM	3267	CD2	PHE	546	47.411	23.730	75.426	1.00	2.00	0
ATOM	3268	CE1	PHE	546	49.127	25.630	76.473	1.00	2.00	0
ATOM	3269	CE2	PHE	546	47.023	25.050	75.496	1.00	2.00	0
ATOM	3270	CZ	PHE	546	47.881	26.006	76.020	1.00	2.00	0
ATOM	3271	C	PHE	546	48.374	19.538	75.658	1.00	2.00	0
ATOM	3272	O	PHE	546	48.141	18.990	74.596	1.00	2.00	0
ATOM	3273	N	LEU	547	49.012	18.935	76.647	1.00	2.00	0
ATOM	3275	CA	LEU	547	49.527	17.582	76.506	1.00	2.00	0
ATOM	3276	CB	LEU	547	50.499	17.289	77.654	1.00	6.91	0
ATOM	3277	CG	LEU	547	51.754	18.159	77.582	1.00	8.40	0
ATOM	3278	CD1	LEU	547	52.096	18.701	78.934	1.00	16.17	0
ATOM	3279	CD2	LEU	547	52.905	17.363	77.029	1.00	11.72	0
ATOM	3280	C	LEU	547	48.422	16.526	76.434	1.00	2.00	0
ATOM	3281	O	LEU	547	48.642	15.414	75.946	1.00	6.91	0
ATOM	3282	N	SER	548	47.230	16.881	76.903	1.00	5.34	0
ATOM	3284	CA	SER	548	46.091	15.964	76.898	1.00	5.34	0
ATOM	3285	CB	SER	548	45.099	16.356	77.993	1.00	36.19	0
ATOM	3286	OG	SER	548	45.611	17.389	78.821	1.00	39.64	0
ATOM	3288	C	SER	548	45.374	15.975	75.552	1.00	5.34	0
ATOM	3289	O	SER	548	44.299	15.381	75.406	1.00	36.66	0
ATOM	3290	N	GLN	549	45.968	16.649	74.569	1.00	23.79	0
ATOM	3292	CA	GLN	549	45.384	16.754	73.242	1.00	23.94	0
ATOM	3293	CB	GLN	549	44.751	18.128	73.084	1.00	46.80	0
ATOM	3294	CG	GLN	549	43.567	18.354	73.990	1.00	38.43	0
ATOM	3295	CD	GLN	549	43.180	19.800	74.054	1.00	38.53	0
ATOM	3296	OE1	GLN	549	43.934	20.672	73.624	1.00	46.42	0
ATOM	3297	NE2	GLN	549	42.002	20.074	74.595	1.00	39.54	0
ATOM	3300	C	GLN	549	46.456	16.547	72.182	1.00	25.87	0
ATOM	3301	O	GLN	549	47.634	16.766	72.451	1.00	42.01	0
ATOM	3302	N	PRO	550	46.068	16.105	70.963	1.00	2.00	0
ATOM	3303	CD	PRO	550	44.729	15.738	70.469	1.00	36.68	0
ATOM	3304	CA	PRO	550	47.075	15.894	69.921	1.00	2.00	0
ATOM	3305	CB	PRO	550	46.253	15.350	68.750	1.00	36.68	0
ATOM	3306	CG	PRO	550	44.886	15.915	68.988	1.00	36.68	0
ATOM	3307	C	PRO	550	47.816	17.184	69.580	1.00	2.00	0
ATOM	3308	O	PRO	550	47.318	18.280	69.840	1.00	36.68	0
ATOM	3309	N	ILE	551	49.013	17.046	69.015	1.00	2.00	0
ATOM	3311	CA	ILE	551	49.824	18.198	68.626	1.00	2.00	0
ATOM	3312	CB	ILE	551	51.293	17.788	68.510	1.00	2.00	0
ATOM	3313	CG2	ILE	551	51.490	16.914	67.292	1.00	2.00	0
ATOM	3314	CG1	ILE	551	52.182	19.021	68.475	1.00	2.00	0

ATOM	3315	CD1	ILE	551	53.648	18.701	68.468	1.00	2.00	0
ATOM	3316	C	ILE	551	49.295	18.705	67.281	1.00	2.00	0
ATOM	3317	O	ILE	551	49.596	19.807	66.840	1.00	2.00	0
ATOM	3318	N	LEU	552	48.514	17.863	66.627	1.00	2.00	0
ATOM	3320	CA	LEU	552	47.896	18.202	65.369	1.00	2.00	0
ATOM	3321	CB	LEU	552	48.287	17.148	64.320	1.00	2.00	0
ATOM	3322	CG	LEU	552	47.809	17.215	62.867	1.00	2.00	0
ATOM	3323	CD1	LEU	552	48.082	18.532	62.209	1.00	2.00	0
ATOM	3324	CD2	LEU	552	48.544	16.174	62.131	1.00	2.00	0
ATOM	3325	C	LEU	552	46.397	18.180	65.728	1.00	2.00	0
ATOM	3326	O	LEU	552	45.753	17.124	65.734	1.00	2.00	0
ATOM	3327	N	LEU	553	45.881	19.352	66.100	1.00	20.15	0
ATOM	3329	CA	LEU	553	44.485	19.512	66.517	1.00	20.15	0
ATOM	3330	CB	LEU	553	44.240	20.926	67.055	1.00	2.00	0
ATOM	3331	CG	LEU	553	44.374	21.262	68.543	1.00	2.00	0
ATOM	3332	CD1	LEU	553	45.224	20.282	69.290	1.00	2.00	0
ATOM	3333	CD2	LEU	553	44.942	22.639	68.638	1.00	2.00	0
ATOM	3334	C	LEU	553	43.495	19.229	65.410	1.00	20.15	0
ATOM	3335	O	LEU	553	43.604	19.780	64.309	1.00	2.00	0
ATOM	3336	N	GLU	554	42.524	18.375	65.724	1.00	14.62	0
ATOM	3338	CA	GLU	554	41.476	17.983	64.786	1.00	13.80	0
ATOM	3339	CB	GLU	554	41.135	16.492	64.956	1.00	57.31	0
ATOM	3340	CG	GLU	554	42.326	15.550	65.177	1.00	69.83	0
ATOM	3341	CD	GLU	554	43.168	15.310	63.927	1.00	73.58	0
ATOM	3342	OE1	GLU	554	42.918	15.957	62.887	1.00	82.45	0
ATOM	3343	OE2	GLU	554	44.090	14.465	63.988	1.00	79.54	0
ATOM	3344	C	GLU	554	40.241	18.823	65.105	1.00	12.33	0
ATOM	3345	O	GLU	554	39.253	18.311	65.638	1.00	51.99	0
ATOM	3346	N	LEU	555	40.296	20.112	64.792	1.00	2.00	0
ATOM	3348	CA	LEU	555	39.176	21.007	65.077	1.00	2.00	0
ATOM	3349	CB	LEU	555	39.628	22.456	64.911	1.00	2.00	0
ATOM	3350	CG	LEU	555	40.660	22.840	65.972	1.00	2.00	0
ATOM	3351	CD1	LEU	555	41.274	24.194	65.697	1.00	2.00	0
ATOM	3352	CD2	LEU	555	39.959	22.839	67.294	1.00	2.00	0
ATOM	3353	C	LEU	555	37.932	20.734	64.237	1.00	2.00	0
ATOM	3354	O	LEU	555	37.862	19.731	63.537	1.00	2.00	0
ATOM	3355	N	GLU	556	36.933	21.603	64.345	1.00	2.00	0
ATOM	3357	CA	GLU	556	35.716	21.460	63.569	1.00	2.00	0
ATOM	3358	CB	GLU	556	35.028	20.115	63.846	1.00	32.90	0
ATOM	3359	CG	GLU	556	34.175	20.063	65.100	1.00	48.42	0
ATOM	3360	CD	GLU	556	32.935	19.176	64.941	1.00	58.49	0
ATOM	3361	OE1	GLU	556	32.792	18.188	65.711	1.00	60.59	0
ATOM	3362	OE2	GLU	556	32.101	19.477	64.047	1.00	59.64	0
ATOM	3363	C	GLU	556	34.736	22.583	63.826	1.00	2.00	0
ATOM	3364	O	GLU	556	35.067	23.580	64.446	1.00	16.83	0
ATOM	3365	N	ALA	557	33.544	22.423	63.257	1.00	2.00	0
ATOM	3367	CA	ALA	557	32.398	23.330	63.427	1.00	2.00	0
ATOM	3368	CB	ALA	557	31.747	23.013	64.788	1.00	47.62	0
ATOM	3369	C	ALA	557	32.701	24.826	63.286	1.00	2.00	0
ATOM	3370	O	ALA	557	33.711	25.191	62.671	1.00	40.85	0
ATOM	3371	N	PRO	558	31.811	25.711	63.802	1.00	2.00	0
ATOM	3372	CD	PRO	558	30.459	25.558	64.353	1.00	2.44	0
ATOM	3373	CA	PRO	558	32.123	27.139	63.658	1.00	2.00	0
ATOM	3374	CB	PRO	558	30.786	27.826	63.951	1.00	2.53	0
ATOM	3375	CG	PRO	558	29.798	26.759	63.843	1.00	2.44	0
ATOM	3376	C	PRO	558	33.190	27.648	64.627	1.00	2.00	0
ATOM	3377	O	PRO	558	32.975	27.616	65.844	1.00	7.53	0
ATOM	3378	N	LEU	559	34.325	28.119	64.112	1.00	2.00	0
ATOM	3380	CA	LEU	559	35.349	28.689	64.982	1.00	2.00	0
ATOM	3381	CB	LEU	559	36.568	27.769	65.148	1.00	2.00	0
ATOM	3382	CG	LEU	559	37.592	27.571	64.050	1.00	2.00	0
ATOM	3383	CD1	LEU	559	38.620	26.563	64.476	1.00	2.00	0
ATOM	3384	CD2	LEU	559	36.885	27.083	62.830	1.00	2.00	0
ATOM	3385	C	LEU	559	35.769	30.038	64.435	1.00	2.00	0
ATOM	3386	O	LEU	559	35.444	30.389	63.311	1.00	2.00	0
ATOM	3387	N	LYS	560	36.461	30.804	65.260	1.00	2.00	0
ATOM	3389	CA	LYS	560	36.932	32.115	64.889	1.00	2.00	0
ATOM	3390	CB	LYS	560	36.359	33.143	65.843	1.00	20.44	0

ATOM	3391	CG	LYS	560	36.612	34.562	65.427	1.00	20.44	0
ATOM	3392	CD	LYS	560	35.574	35.512	66.018	1.00	20.44	0
ATOM	3393	CE	LYS	560	34.253	35.452	65.278	1.00	20.44	0
ATOM	3394	NZ	LYS	560	33.706	34.083	65.225	1.00	20.44	0
ATOM	3398	C	LYS	560	38.426	31.990	65.052	1.00	2.00	0
ATOM	3399	O	LYS	560	38.908	31.624	66.117	1.00	20.44	0
ATOM	3400	N	ILE	561	39.164	32.244	63.986	1.00	2.00	0
ATOM	3402	CA	ILE	561	40.606	32.106	64.017	1.00	2.00	0
ATOM	3403	CB	ILE	561	41.095	31.318	62.750	1.00	2.00	0
ATOM	3404	CG2	ILE	561	42.566	30.913	62.891	1.00	2.00	0
ATOM	3405	CG1	ILE	561	40.204	30.076	62.558	1.00	2.00	0
ATOM	3406	CD1	ILE	561	40.806	28.940	61.761	1.00	2.00	0
ATOM	3407	C	ILE	561	41.247	33.488	64.102	1.00	2.00	0
ATOM	3408	O	ILE	561	40.703	34.450	63.543	1.00	2.00	0
ATOM	3409	N	CYS	562	42.365	33.586	64.833	1.00	2.00	0
ATOM	3411	CA	CYS	562	43.124	34.829	65.001	1.00	2.00	0
ATOM	3412	CB	CYS	562	42.793	35.464	66.339	1.00	13.31	0
ATOM	3413	SG	CYS	562	41.073	35.733	66.574	1.00	13.31	0
ATOM	3414	C	CYS	562	44.642	34.589	64.928	1.00	2.00	0
ATOM	3415	O	CYS	562	45.151	33.551	65.373	1.00	13.31	0
ATOM	3416	N	GLY	563	45.362	35.540	64.348	1.00	2.00	0
ATOM	3418	CA	GLY	563	46.805	35.424	64.252	1.00	2.00	0
ATOM	3419	C	GLY	563	47.546	36.260	65.291	1.00	2.00	0
ATOM	3420	O	GLY	563	46.997	36.556	66.351	1.00	5.66	0
ATOM	3421	N	ASP	564	48.780	36.649	64.958	1.00	2.00	0
ATOM	3423	CA	ASP	564	49.657	37.452	65.811	1.00	2.00	0
ATOM	3424	CB	ASP	564	50.705	38.191	64.964	1.00	2.00	0
ATOM	3425	CG	ASP	564	51.724	37.270	64.321	1.00	2.00	0
ATOM	3426	OD1	ASP	564	51.390	36.585	63.334	1.00	2.00	0
ATOM	3427	OD2	ASP	564	52.876	37.249	64.786	1.00	2.00	0
ATOM	3428	C	ASP	564	48.981	38.497	66.693	1.00	2.00	0
ATOM	3429	O	ASP	564	48.395	39.442	66.189	1.00	2.00	0
ATOM	3430	N	ILE	565	49.094	38.327	68.009	1.00	31.53	0
ATOM	3432	CA	ILE	565	48.537	39.294	68.953	1.00	35.54	0
ATOM	3433	CB	ILE	565	47.810	38.612	70.135	1.00	9.39	0
ATOM	3434	CG2	ILE	565	47.139	39.664	70.996	1.00	9.39	0
ATOM	3435	CG1	ILE	565	46.710	37.685	69.622	1.00	9.39	0
ATOM	3436	CD1	ILE	565	45.611	38.424	68.906	1.00	9.39	0
ATOM	3437	C	ILE	565	49.681	40.168	69.489	1.00	32.16	0
ATOM	3438	O	ILE	565	49.491	41.356	69.756	1.00	9.39	0
ATOM	3439	N	HIS	566	50.859	39.560	69.637	1.00	14.33	0
ATOM	3441	CA	HIS	566	52.082	40.219	70.111	1.00	15.67	0
ATOM	3442	C	HIS	566	51.958	41.227	71.245	1.00	16.54	0
ATOM	3443	O	HIS	566	52.427	42.359	71.127	1.00	15.89	0
ATOM	3444	CB	HIS	566	52.811	40.882	68.943	1.00	9.53	0
ATOM	3445	CG	HIS	566	53.652	39.936	68.153	1.00	9.53	0
ATOM	3446	ND1	HIS	566	54.829	39.391	68.605	1.00	9.53	0
ATOM	3448	CD2	HIS	566	53.470	39.432	66.910	1.00	9.53	0
ATOM	3449	NE2	HIS	566	54.525	38.582	66.589	1.00	9.53	0
ATOM	3450	CE1	HIS	566	55.312	38.600	67.652	1.00	9.53	0
ATOM	3451	N	GLY	567	51.337	40.808	72.345	1.00	2.00	0
ATOM	3453	CA	GLY	567	51.170	41.686	73.490	1.00	2.00	0
ATOM	3454	C	GLY	567	50.249	42.894	73.375	1.00	2.00	0
ATOM	3455	O	GLY	567	50.269	43.764	74.254	1.00	3.59	0
ATOM	3456	N	GLN	568	49.455	42.973	72.314	1.00	36.66	0
ATOM	3458	CA	GLN	568	48.527	44.086	72.141	1.00	34.60	0
ATOM	3459	CB	GLN	568	48.164	44.236	70.667	1.00	2.50	0
ATOM	3460	CG	GLN	568	49.345	44.164	69.715	1.00	3.37	0
ATOM	3461	CD	GLN	568	49.768	45.507	69.144	1.00	3.10	0
ATOM	3462	OE1	GLN	568	50.958	45.769	68.974	1.00	4.87	0
ATOM	3463	NE2	GLN	568	48.800	46.349	68.813	1.00	18.91	0
ATOM	3466	C	GLN	568	47.280	43.730	72.950	1.00	34.26	0
ATOM	3467	O	GLN	568	46.253	43.365	72.380	1.00	7.33	0
ATOM	3468	N	TYR	569	47.363	43.864	74.272	1.00	2.00	0
ATOM	3470	CA	TYR	569	46.263	43.485	75.161	1.00	2.00	0
ATOM	3471	CB	TYR	569	46.664	43.687	76.626	1.00	26.93	0
ATOM	3472	CG	TYR	569	45.692	43.048	77.600	1.00	27.02	0
ATOM	3473	CD1	TYR	569	45.401	41.684	77.526	1.00	22.43	0

ATOM	3474	CE1	TYR	569	44.496	41.097	78.393	1.00	24.12	0
ATOM	3475	CD2	TYR	569	45.049	43.807	78.575	1.00	24.68	0
ATOM	3476	CE2	TYR	569	44.139	43.223	79.449	1.00	24.01	0
ATOM	3477	CZ	TYR	569	43.866	41.869	79.352	1.00	28.35	0
ATOM	3478	OH	TYR	569	42.950	41.282	80.197	1.00	35.43	0
ATOM	3480	C	TYR	569	44.888	44.085	74.946	1.00	2.00	0
ATOM	3481	O	TYR	569	43.885	43.374	75.015	1.00	29.07	0
ATOM	3482	N	TYR	570	44.817	45.384	74.710	1.00	11.04	0
ATOM	3484	CA	TYR	570	43.515	45.999	74.510	1.00	14.25	0
ATOM	3485	CB	TYR	570	43.599	47.505	74.766	1.00	46.12	0
ATOM	3486	CG	TYR	570	43.577	47.792	76.261	1.00	51.43	0
ATOM	3487	CD1	TYR	570	44.749	47.743	77.025	1.00	48.11	0
ATOM	3488	CE1	TYR	570	44.715	47.952	78.398	1.00	52.04	0
ATOM	3489	CD2	TYR	570	42.375	48.063	76.917	1.00	49.50	0
ATOM	3490	CE2	TYR	570	42.340	48.272	78.277	1.00	51.48	0
ATOM	3491	CZ	TYR	570	43.507	48.215	79.010	1.00	53.24	0
ATOM	3492	OH	TYR	570	43.452	48.426	80.359	1.00	54.97	0
ATOM	3494	C	TYR	570	42.929	45.653	73.152	1.00	13.58	0
ATOM	3495	O	TYR	570	41.708	45.654	72.967	1.00	43.14	0
ATOM	3496	N	ASP	571	43.813	45.311	72.217	1.00	12.28	0
ATOM	3498	CA	ASP	571	43.402	44.903	70.891	1.00	11.58	0
ATOM	3499	CB	ASP	571	44.590	44.870	69.975	1.00	6.85	0
ATOM	3500	CG	ASP	571	45.128	46.237	69.733	1.00	12.88	0
ATOM	3501	OD1	ASP	571	46.254	46.522	70.185	1.00	19.21	0
ATOM	3502	OD2	ASP	571	44.402	47.044	69.110	1.00	16.01	0
ATOM	3503	C	ASP	571	42.818	43.539	71.062	1.00	14.93	0
ATOM	3504	O	ASP	571	41.775	43.247	70.507	1.00	19.59	0
ATOM	3505	N	LEU	572	43.487	42.707	71.853	1.00	2.00	0
ATOM	3507	CA	LEU	572	42.977	41.378	72.147	1.00	2.00	0
ATOM	3508	CB	LEU	572	43.909	40.641	73.110	1.00	2.00	0
ATOM	3509	CG	LEU	572	43.302	39.416	73.820	1.00	2.00	0
ATOM	3510	CD1	LEU	572	43.061	38.267	72.832	1.00	2.00	0
ATOM	3511	CD2	LEU	572	44.227	38.982	74.955	1.00	2.00	0
ATOM	3512	C	LEU	572	41.579	41.554	72.771	1.00	2.00	0
ATOM	3513	O	LEU	572	40.678	40.758	72.512	1.00	2.00	0
ATOM	3514	N	LEU	573	41.395	42.604	73.572	1.00	9.95	0
ATOM	3516	CA	LEU	573	40.092	42.874	74.195	1.00	6.25	0
ATOM	3517	CB	LEU	573	40.224	43.910	75.317	1.00	2.00	0
ATOM	3518	CG	LEU	573	40.807	43.360	76.625	1.00	2.00	0
ATOM	3519	CD1	LEU	573	40.667	44.416	77.717	1.00	2.00	0
ATOM	3520	CD2	LEU	573	40.079	42.053	77.033	1.00	2.00	0
ATOM	3521	C	LEU	573	39.055	43.344	73.170	1.00	4.08	0
ATOM	3522	O	LEU	573	37.865	42.974	73.260	1.00	2.00	0
ATOM	3523	N	ARG	574	39.518	44.153	72.203	1.00	13.12	0
ATOM	3525	CA	ARG	574	38.682	44.665	71.115	1.00	12.30	0
ATOM	3526	CB	ARG	574	39.491	45.598	70.212	1.00	30.04	0
ATOM	3527	CG	ARG	574	39.704	46.994	70.757	1.00	31.00	0
ATOM	3528	CD	ARG	574	40.697	47.811	69.915	1.00	35.07	0
ATOM	3529	NE	ARG	574	40.294	47.989	68.514	1.00	36.10	0
ATOM	3531	CZ	ARG	574	41.018	48.625	67.587	1.00	36.14	0
ATOM	3532	NH1	ARG	574	42.198	49.162	67.890	1.00	35.84	0
ATOM	3535	NH2	ARG	574	40.565	48.713	66.341	1.00	40.46	0
ATOM	3538	C	ARG	574	38.265	43.440	70.324	1.00	10.99	0
ATOM	3539	O	ARG	574	37.092	43.253	70.004	1.00	30.16	0
ATOM	3540	N	LEU	575	39.260	42.591	70.066	1.00	2.00	0
ATOM	3542	CA	LEU	575	39.156	41.339	69.323	1.00	2.00	0
ATOM	3543	CB	LEU	575	40.471	40.578	69.502	1.00	18.14	0
ATOM	3544	CG	LEU	575	41.058	39.569	68.514	1.00	18.14	0
ATOM	3545	CD1	LEU	575	40.112	38.378	68.370	1.00	18.14	0
ATOM	3546	CD2	LEU	575	41.355	40.249	67.176	1.00	18.14	0
ATOM	3547	C	LEU	575	37.970	40.494	69.801	1.00	2.00	0
ATOM	3548	O	LEU	575	37.121	40.081	69.001	1.00	18.14	0
ATOM	3549	N	PHE	576	37.908	40.247	71.103	1.00	29.25	0
ATOM	3551	CA	PHE	576	36.823	39.459	71.664	1.00	32.60	0
ATOM	3552	CB	PHE	576	37.115	39.098	73.119	1.00	2.00	0
ATOM	3553	CG	PHE	576	38.116	38.001	73.270	1.00	2.00	0
ATOM	3554	CD1	PHE	576	39.158	38.111	74.184	1.00	2.00	0
ATOM	3555	CD2	PHE	576	38.022	36.855	72.491	1.00	2.00	0

ATOM	3556	CE1	PHE	576	40.097	37.098	74.324	1.00	2.00	0
ATOM	3557	CE2	PHE	576	38.960	35.828	72.621	1.00	2.00	0
ATOM	3558	CZ	PHE	576	40.000	35.953	73.540	1.00	2.00	0
ATOM	3559	C	PHE	576	35.479	40.164	71.573	1.00	29.95	0
ATOM	3560	O	PHE	576	34.433	39.517	71.648	1.00	2.00	0
ATOM	3561	N	GLU	577	35.504	41.484	71.421	1.00	21.04	0
ATOM	3563	CA	GLU	577	34.273	42.259	71.307	1.00	23.58	0
ATOM	3564	CB	GLU	577	34.561	43.731	71.566	1.00	40.21	0
ATOM	3565	CG	GLU	577	35.032	44.001	72.971	1.00	50.88	0
ATOM	3566	CD	GLU	577	35.688	45.347	73.113	1.00	55.67	0
ATOM	3567	OE1	GLU	577	36.439	45.522	74.099	1.00	60.01	0
ATOM	3568	OE2	GLU	577	35.461	46.224	72.245	1.00	63.14	0
ATOM	3569	C	GLU	577	33.654	42.091	69.928	1.00	25.67	0
ATOM	3570	O	GLU	577	32.435	42.156	69.772	1.00	44.83	0
ATOM	3571	N	TYR	578	34.509	41.901	68.928	1.00	51.92	0
ATOM	3573	CA	TYR	578	34.052	41.700	67.561	1.00	48.79	0
ATOM	3574	CB	TYR	578	35.208	41.834	66.564	1.00	35.56	0
ATOM	3575	CG	TYR	578	35.703	43.245	66.356	1.00	40.25	0
ATOM	3576	CD1	TYR	578	35.598	43.865	65.111	1.00	40.27	0
ATOM	3577	CE1	TYR	578	36.062	45.168	64.917	1.00	44.74	0
ATOM	3578	CD2	TYR	578	36.281	43.960	67.399	1.00	45.71	0
ATOM	3579	CE2	TYR	578	36.747	45.258	67.217	1.00	42.53	0
ATOM	3580	CZ	TYR	578	36.636	45.853	65.979	1.00	49.98	0
ATOM	3581	OH	TYR	578	37.106	47.131	65.812	1.00	54.82	0
ATOM	3583	C	TYR	578	33.467	40.303	67.458	1.00	49.18	0
ATOM	3584	O	TYR	578	32.316	40.124	67.081	1.00	35.27	0
ATOM	3585	N	GLY	579	34.271	39.307	67.797	1.00	2.60	0
ATOM	3587	CA	GLY	579	33.787	37.949	67.713	1.00	6.22	0
ATOM	3588	C	GLY	579	32.737	37.628	68.755	1.00	8.52	0
ATOM	3589	O	GLY	579	31.555	37.446	68.437	1.00	39.88	0
ATOM	3590	N	GLY	580	33.194	37.557	70.006	1.00	2.00	0
ATOM	3592	CA	GLY	580	32.342	37.236	71.140	1.00	2.00	0
ATOM	3593	C	GLY	580	33.191	36.491	72.151	1.00	2.00	0
ATOM	3594	O	GLY	580	33.725	35.415	71.853	1.00	44.94	0
ATOM	3595	N	PHE	581	33.307	37.067	73.348	1.00	15.06	0
ATOM	3597	CA	PHE	581	34.116	36.500	74.432	1.00	12.63	0
ATOM	3598	CB	PHE	581	33.857	37.263	75.744	1.00	2.00	0
ATOM	3599	CG	PHE	581	34.679	38.542	75.885	1.00	2.00	0
ATOM	3600	CD1	PHE	581	34.136	39.783	75.557	1.00	2.00	0
ATOM	3601	CD2	PHE	581	35.999	38.495	76.346	1.00	2.00	0
ATOM	3602	CE1	PHE	581	34.894	40.941	75.687	1.00	2.00	0
ATOM	3603	CE2	PHE	581	36.757	39.659	76.475	1.00	2.00	0
ATOM	3604	CZ	PHE	581	36.204	40.875	76.146	1.00	2.00	0
ATOM	3605	C	PHE	581	33.913	34.999	74.611	1.00	12.63	0
ATOM	3606	O	PHE	581	32.782	34.521	74.647	1.00	2.00	0
ATOM	3607	N	PRO	582	35.021	34.243	74.737	1.00	21.81	0
ATOM	3608	CD	PRO	582	36.360	34.852	74.820	1.00	85.20	0
ATOM	3609	CA	PRO	582	35.141	32.795	74.910	1.00	24.62	0
ATOM	3610	CB	PRO	582	36.398	32.675	75.737	1.00	86.40	0
ATOM	3611	CG	PRO	582	37.266	33.636	75.008	1.00	87.84	0
ATOM	3612	C	PRO	582	33.966	31.958	75.425	1.00	28.53	0
ATOM	3613	O	PRO	582	33.816	30.796	75.012	1.00	0.58	0
ATOM	3614	N	PRO	583	33.160	32.466	76.374	1.00	13.00	0
ATOM	3615	CD	PRO	583	33.090	33.632	77.269	1.00	51.24	0
ATOM	3616	CA	PRO	583	32.099	31.500	76.681	1.00	13.55	0
ATOM	3617	CB	PRO	583	31.281	32.215	77.759	1.00	53.59	0
ATOM	3618	CG	PRO	583	31.616	33.699	77.550	1.00	50.46	0
ATOM	3619	C	PRO	583	31.296	31.283	75.389	1.00	14.03	0
ATOM	3620	O	PRO	583	30.950	30.152	75.043	1.00	48.29	0
ATOM	3621	N	GLU	584	31.089	32.383	74.663	1.00	35.81	0
ATOM	3623	CA	GLU	584	30.333	32.439	73.412	1.00	39.44	0
ATOM	3624	CB	GLU	584	30.122	33.913	73.043	1.00	78.69	0
ATOM	3625	CG	GLU	584	28.955	34.213	72.117	1.00	90.10	0
ATOM	3626	CD	GLU	584	28.662	35.712	72.022	1.00	95.41	0
ATOM	3627	OE1	GLU	584	28.313	36.190	70.918	1.00	90.41	0
ATOM	3628	OE2	GLU	584	28.782	36.418	73.053	1.00	95.81	0
ATOM	3629	C	GLU	584	30.975	31.676	72.244	1.00	36.17	0
ATOM	3630	O	GLU	584	30.780	30.466	72.106	1.00	78.35	0

ATOM	3631	N	SER	585	31.737	32.381	71.406	1.00	12.28	0
ATOM	3633	CA	SER	585	32.394	31.779	70.245	1.00	8.77	0
ATOM	3634	CB	SER	585	32.720	32.857	69.209	1.00	31.98	0
ATOM	3635	OG	SER	585	31.558	33.556	68.809	1.00	27.38	0
ATOM	3637	C	SER	585	33.669	30.995	70.539	1.00	9.84	0
ATOM	3638	O	SER	585	34.382	31.258	71.502	1.00	35.35	0
ATOM	3639	N	ASN	586	33.947	30.037	69.664	1.00	2.00	0
ATOM	3641	CA	ASN	586	35.136	29.197	69.749	1.00	2.00	0
ATOM	3642	CB	ASN	586	34.909	27.854	69.068	1.00	2.87	0
ATOM	3643	CG	ASN	586	33.728	27.107	69.625	1.00	10.37	0
ATOM	3644	OD1	ASN	586	33.497	25.960	69.265	1.00	11.13	0
ATOM	3645	ND2	ASN	586	32.967	27.745	70.506	1.00	4.44	0
ATOM	3648	C	ASN	586	36.251	29.937	69.029	1.00	2.00	0
ATOM	3649	O	ASN	586	36.017	30.574	68.007	1.00	2.87	0
ATOM	3650	N	TYR	587	37.458	29.858	69.564	1.00	13.99	0
ATOM	3652	CA	TYR	587	38.571	30.554	68.966	1.00	13.99	0
ATOM	3653	CB	TYR	587	39.049	31.706	69.876	1.00	2.00	0
ATOM	3654	CG	TYR	587	38.177	32.946	69.873	1.00	2.00	0
ATOM	3655	CD1	TYR	587	36.998	33.004	70.638	1.00	2.00	0
ATOM	3656	CE1	TYR	587	36.177	34.138	70.624	1.00	2.00	0
ATOM	3657	CD2	TYR	587	38.519	34.061	69.088	1.00	2.00	0
ATOM	3658	CE2	TYR	587	37.701	35.205	69.065	1.00	2.00	0
ATOM	3659	CZ	TYR	587	36.532	35.231	69.840	1.00	2.00	0
ATOM	3660	OH	TYR	587	35.743	36.352	69.838	1.00	2.00	0
ATOM	3662	C	TYR	587	39.721	29.608	68.745	1.00	13.99	0
ATOM	3663	O	TYR	587	39.812	28.562	69.392	1.00	2.00	0
ATOM	3664	N	LEU	588	40.584	29.987	67.809	1.00	2.00	0
ATOM	3666	CA	LEU	588	41.803	29.261	67.493	1.00	2.00	0
ATOM	3667	CB	LEU	588	41.681	28.482	66.195	1.00	10.69	0
ATOM	3668	CG	LEU	588	43.032	27.907	65.781	1.00	10.69	0
ATOM	3669	CD1	LEU	588	43.568	27.073	66.912	1.00	10.69	0
ATOM	3670	CD2	LEU	588	42.912	27.079	64.533	1.00	10.69	0
ATOM	3671	C	LEU	588	42.809	30.375	67.301	1.00	2.00	0
ATOM	3672	O	LEU	588	42.547	31.301	66.532	1.00	10.69	0
ATOM	3673	N	PHE	589	43.924	30.333	68.026	1.00	2.00	0
ATOM	3675	CA	PHE	589	44.938	31.363	67.865	1.00	2.00	0
ATOM	3676	CB	PHE	589	45.289	32.013	69.200	1.00	2.00	0
ATOM	3677	CG	PHE	589	44.279	33.026	69.652	1.00	2.00	0
ATOM	3678	CD1	PHE	589	43.136	32.633	70.326	1.00	2.00	0
ATOM	3679	CD2	PHE	589	44.471	34.376	69.391	1.00	2.00	0
ATOM	3680	CE1	PHE	589	42.203	33.567	70.732	1.00	2.00	0
ATOM	3681	CE2	PHE	589	43.542	35.321	69.793	1.00	2.00	0
ATOM	3682	CZ	PHE	589	42.408	34.918	70.463	1.00	2.00	0
ATOM	3683	C	PHE	589	46.140	30.717	67.219	1.00	2.00	0
ATOM	3684	O	PHE	589	46.532	29.610	67.602	1.00	2.00	0
ATOM	3685	N	LEU	590	46.715	31.411	66.235	1.00	2.00	0
ATOM	3687	CA	LEU	590	47.845	30.892	65.459	1.00	2.00	0
ATOM	3688	CB	LEU	590	47.650	31.303	63.988	1.00	9.73	0
ATOM	3689	CG	LEU	590	46.273	31.022	63.356	1.00	9.73	0
ATOM	3690	CD1	LEU	590	46.162	31.702	62.014	1.00	9.73	0
ATOM	3691	CD2	LEU	590	46.056	29.529	63.211	1.00	9.73	0
ATOM	3692	C	LEU	590	49.277	31.221	65.947	1.00	2.00	0
ATOM	3693	O	LEU	590	50.263	30.856	65.296	1.00	9.73	0
ATOM	3694	N	GLY	591	49.389	31.929	67.071	1.00	2.00	0
ATOM	3696	CA	GLY	591	50.703	32.223	67.626	1.00	2.00	0
ATOM	3697	C	GLY	591	51.132	33.648	67.923	1.00	2.00	0
ATOM	3698	O	GLY	591	50.369	34.620	67.769	1.00	2.00	0
ATOM	3699	N	ASP	592	52.387	33.741	68.358	1.00	2.00	0
ATOM	3701	CA	ASP	592	53.033	35.000	68.707	1.00	2.00	0
ATOM	3702	CB	ASP	592	53.424	35.746	67.448	1.00	6.15	0
ATOM	3703	CG	ASP	592	54.521	35.051	66.686	1.00	16.84	0
ATOM	3704	OD1	ASP	592	54.955	35.606	65.657	1.00	11.71	0
ATOM	3705	OD2	ASP	592	54.943	33.949	67.114	1.00	18.80	0
ATOM	3706	C	ASP	592	52.194	35.887	69.598	1.00	2.00	0
ATOM	3707	O	ASP	592	51.813	36.995	69.211	1.00	6.68	0
ATOM	3708	N	TYR	593	51.927	35.370	70.800	1.00	12.61	0
ATOM	3710	CA	TYR	593	51.127	36.036	71.822	1.00	12.61	0
ATOM	3711	CB	TYR	593	50.602	35.017	72.827	1.00	2.00	0

ATOM	3712	CG	TYR	593	49.994	33.790	72.200	1.00	2.00	0
ATOM	3713	CD1	TYR	593	50.558	32.532	72.382	1.00	2.00	0
ATOM	3714	CE1	TYR	593	49.995	31.401	71.793	1.00	2.00	0
ATOM	3715	CD2	TYR	593	48.852	33.886	71.413	1.00	2.00	0
ATOM	3716	CE2	TYR	593	48.284	32.772	70.822	1.00	2.00	0
ATOM	3717	CZ	TYR	593	48.856	31.540	71.013	1.00	2.00	0
ATOM	3718	OH	TYR	593	48.267	30.459	70.412	1.00	2.00	0
ATOM	3720	C	TYR	593	51.995	37.019	72.560	1.00	12.61	0
ATOM	3721	O	TYR	593	51.526	38.079	72.981	1.00	2.00	0
ATOM	3722	N	VAL	594	53.270	36.660	72.692	1.00	2.00	0
ATOM	3724	CA	VAL	594	54.238	37.463	73.420	1.00	2.00	0
ATOM	3725	CB	VAL	594	54.913	36.599	74.501	1.00	30.06	0
ATOM	3726	CG1	VAL	594	53.855	35.785	75.241	1.00	30.06	0
ATOM	3727	CG2	VAL	594	55.950	35.684	73.875	1.00	30.06	0
ATOM	3728	C	VAL	594	55.309	38.154	72.563	1.00	2.00	0
ATOM	3729	O	VAL	594	55.408	37.919	71.356	1.00	30.06	0
ATOM	3730	N	ASP	595	56.112	38.991	73.218	1.00	2.00	0
ATOM	3732	CA	ASP	595	57.184	39.776	72.601	1.00	2.00	0
ATOM	3733	CB	ASP	595	58.073	38.903	71.705	1.00	33.25	0
ATOM	3734	CG	ASP	595	58.911	37.890	72.502	1.00	42.03	0
ATOM	3735	OD1	ASP	595	59.240	38.147	73.679	1.00	40.72	0
ATOM	3736	OD2	ASP	595	59.256	36.831	71.941	1.00	46.45	0
ATOM	3737	C	ASP	595	56.547	40.920	71.818	1.00	2.00	0
ATOM	3738	O	ASP	595	55.335	40.901	71.575	1.00	29.29	0
ATOM	3739	N	ARG	596	57.342	41.927	71.460	1.00	2.00	0
ATOM	3741	CA	ARG	596	56.843	43.096	70.716	1.00	2.00	0
ATOM	3742	CB	ARG	596	56.146	42.658	69.416	1.00	7.10	0
ATOM	3743	CG	ARG	596	57.043	41.863	68.457	1.00	13.06	0
ATOM	3744	CD	ARG	596	58.035	42.755	67.729	1.00	17.94	0
ATOM	3745	NE	ARG	596	59.293	42.081	67.407	1.00	25.56	0
ATOM	3747	CZ	ARG	596	59.402	40.954	66.709	1.00	35.06	0
ATOM	3748	NH1	ARG	596	58.325	40.338	66.236	1.00	31.67	0
ATOM	3751	NH2	ARG	596	60.604	40.438	66.486	1.00	31.81	0
ATOM	3754	C	ARG	596	55.898	43.996	71.547	1.00	2.00	0
ATOM	3755	O	ARG	596	56.269	45.112	71.922	1.00	7.10	0
ATOM	3756	N	GLY	597	54.692	43.521	71.847	1.00	32.20	0
ATOM	3758	CA	GLY	597	53.763	44.323	72.632	1.00	30.86	0
ATOM	3759	C	GLY	597	54.199	44.603	74.062	1.00	35.68	0
ATOM	3760	O	GLY	597	55.120	43.976	74.570	1.00	2.00	0
ATOM	3761	N	LYS	598	53.520	45.539	74.720	1.00	20.71	0
ATOM	3763	CA	LYS	598	53.845	45.911	76.097	1.00	17.90	0
ATOM	3764	CB	LYS	598	53.686	47.427	76.271	1.00	54.79	0
ATOM	3765	CG	LYS	598	54.813	48.259	75.655	1.00	53.06	0
ATOM	3766	CD	LYS	598	56.159	48.031	76.359	1.00	56.27	0
ATOM	3767	CE	LYS	598	56.120	48.441	77.838	1.00	53.59	0
ATOM	3768	NZ	LYS	598	57.407	48.186	78.548	1.00	56.50	0
ATOM	3772	C	LYS	598	53.064	45.179	77.210	1.00	18.19	0
ATOM	3773	O	LYS	598	53.384	45.314	78.395	1.00	55.50	0
ATOM	3774	N	GLN	599	52.053	44.400	76.832	1.00	2.00	0
ATOM	3776	CA	GLN	599	51.244	43.666	77.795	1.00	2.00	0
ATOM	3777	CB	GLN	599	49.820	44.244	77.839	1.00	24.44	0
ATOM	3778	CG	GLN	599	49.780	45.701	78.304	1.00	31.08	0
ATOM	3779	CD	GLN	599	48.398	46.169	78.728	1.00	27.33	0
ATOM	3780	OE1	GLN	599	47.537	46.449	77.895	1.00	26.31	0
ATOM	3781	NE2	GLN	599	48.188	46.277	80.029	1.00	27.77	0
ATOM	3784	C	GLN	599	51.215	42.163	77.514	1.00	2.00	0
ATOM	3785	O	GLN	599	50.183	41.515	77.626	1.00	24.92	0
ATOM	3786	N	SER	600	52.371	41.602	77.198	1.00	2.00	0
ATOM	3788	CA	SER	600	52.445	40.180	76.921	1.00	2.00	0
ATOM	3789	CB	SER	600	53.875	39.781	76.547	1.00	2.00	0
ATOM	3790	OG	SER	600	54.381	40.577	75.480	1.00	2.00	0
ATOM	3792	C	SER	600	51.968	39.304	78.078	1.00	2.00	0
ATOM	3793	O	SER	600	51.589	38.153	77.856	1.00	2.00	0
ATOM	3794	N	LEU	601	51.990	39.830	79.306	1.00	2.00	0
ATOM	3796	CA	LEU	601	51.566	39.055	80.486	1.00	2.00	0
ATOM	3797	CB	LEU	601	52.120	39.628	81.801	1.00	2.00	0
ATOM	3798	CG	LEU	601	53.573	39.753	82.260	1.00	2.00	0
ATOM	3799	CD1	LEU	601	54.290	38.405	82.228	1.00	2.00	0

ATOM	3800	CD2	LEU	601	54.244	40.799	81.399	1.00	2.00	0
ATOM	3801	C	LEU	601	50.058	39.002	80.635	1.00	2.00	0
ATOM	3802	O	LEU	601	49.498	37.949	80.921	1.00	4.13	0
ATOM	3803	N	GLU	602	49.412	40.154	80.490	1.00	2.00	0
ATOM	3805	CA	GLU	602	47.969	40.227	80.608	1.00	2.00	0
ATOM	3806	CB	GLU	602	47.486	41.676	80.495	1.00	5.18	0
ATOM	3807	CG	GLU	602	47.752	42.552	81.739	1.00	5.18	0
ATOM	3808	CD	GLU	602	49.152	43.180	81.773	1.00	5.18	0
ATOM	3809	OE1	GLU	602	50.146	42.439	81.854	1.00	5.18	0
ATOM	3810	OE2	GLU	602	49.266	44.424	81.732	1.00	5.18	0
ATOM	3811	C	GLU	602	47.413	39.391	79.479	1.00	2.00	0
ATOM	3812	O	GLU	602	46.452	38.661	79.661	1.00	5.18	0
ATOM	3813	N	THR	603	48.072	39.477	78.323	1.00	56.10	0
ATOM	3815	CA	THR	603	47.705	38.748	77.110	1.00	56.10	0
ATOM	3816	CB	THR	603	48.585	39.206	75.941	1.00	8.67	0
ATOM	3817	OG1	THR	603	48.197	40.527	75.557	1.00	8.67	0
ATOM	3819	CG2	THR	603	48.437	38.272	74.748	1.00	8.67	0
ATOM	3820	C	THR	603	47.794	37.228	77.228	1.00	56.10	0
ATOM	3821	O	THR	603	46.804	36.522	77.060	1.00	8.67	0
ATOM	3822	N	ILE	604	48.980	36.713	77.505	1.00	2.00	0
ATOM	3824	CA	ILE	604	49.137	35.273	77.630	1.00	2.00	0
ATOM	3825	CB	ILE	604	50.643	34.900	77.738	1.00	2.00	0
ATOM	3826	CG2	ILE	604	51.244	35.475	79.009	1.00	2.00	0
ATOM	3827	CG1	ILE	604	50.812	33.382	77.627	1.00	2.00	0
ATOM	3828	CD1	ILE	604	50.177	32.766	76.369	1.00	2.00	0
ATOM	3829	C	ILE	604	48.314	34.710	78.808	1.00	2.00	0
ATOM	3830	O	ILE	604	47.886	33.565	78.779	1.00	2.00	0
ATOM	3831	N	CYS	605	48.057	35.526	79.821	1.00	17.68	0
ATOM	3833	CA	CYS	605	47.283	35.072	80.962	1.00	16.48	0
ATOM	3834	CB	CYS	605	47.434	36.026	82.138	1.00	12.63	0
ATOM	3835	SG	CYS	605	48.994	35.843	82.980	1.00	18.12	0
ATOM	3836	C	CYS	605	45.824	34.923	80.630	1.00	10.22	0
ATOM	3837	O	CYS	605	45.185	33.963	81.068	1.00	8.59	0
ATOM	3838	N	LEU	606	45.280	35.856	79.861	1.00	2.00	0
ATOM	3840	CA	LEU	606	43.874	35.771	79.504	1.00	2.00	0
ATOM	3841	CB	LEU	606	43.396	37.087	78.881	1.00	2.00	0
ATOM	3842	CG	LEU	606	41.886	37.223	78.636	1.00	2.00	0
ATOM	3843	CD1	LEU	606	41.081	36.716	79.867	1.00	2.00	0
ATOM	3844	CD2	LEU	606	41.551	38.688	78.326	1.00	2.00	0
ATOM	3845	C	LEU	606	43.589	34.599	78.559	1.00	2.00	0
ATOM	3846	O	LEU	606	42.503	34.012	78.612	1.00	2.00	0
ATOM	3847	N	LEU	607	44.562	34.246	77.713	1.00	9.59	0
ATOM	3849	CA	LEU	607	44.392	33.137	76.772	1.00	9.59	0
ATOM	3850	CB	LEU	607	45.394	33.246	75.604	1.00	9.66	0
ATOM	3851	CG	LEU	607	45.302	34.531	74.755	1.00	9.66	0
ATOM	3852	CD1	LEU	607	46.376	34.564	73.709	1.00	9.66	0
ATOM	3853	CD2	LEU	607	43.951	34.634	74.114	1.00	9.66	0
ATOM	3854	C	LEU	607	44.509	31.781	77.476	1.00	9.59	0
ATOM	3855	O	LEU	607	43.772	30.841	77.148	1.00	9.66	0
ATOM	3856	N	LEU	608	45.412	31.688	78.452	1.00	67.56	0
ATOM	3858	CA	LEU	608	45.599	30.460	79.230	1.00	67.56	0
ATOM	3859	CB	LEU	608	46.872	30.529	80.054	1.00	2.00	0
ATOM	3860	CG	LEU	608	48.168	30.385	79.273	1.00	2.00	0
ATOM	3861	CD1	LEU	608	49.357	30.366	80.234	1.00	2.00	0
ATOM	3862	CD2	LEU	608	48.109	29.107	78.462	1.00	2.00	0
ATOM	3863	C	LEU	608	44.427	30.217	80.170	1.00	67.56	0
ATOM	3864	O	LEU	608	44.097	29.059	80.477	1.00	2.00	0
ATOM	3865	N	ALA	609	43.833	31.313	80.653	1.00	2.00	0
ATOM	3867	CA	ALA	609	42.667	31.250	81.531	1.00	2.00	0
ATOM	3868	CB	ALA	609	42.322	32.637	82.044	1.00	2.00	0
ATOM	3869	C	ALA	609	41.496	30.677	80.734	1.00	2.00	0
ATOM	3870	O	ALA	609	40.833	29.747	81.162	1.00	2.00	0
ATOM	3871	N	TYR	610	41.263	31.231	79.552	1.00	2.00	0
ATOM	3873	CA	TYR	610	40.186	30.771	78.686	1.00	2.00	0
ATOM	3874	CB	TYR	610	40.046	31.717	77.504	1.00	2.00	0
ATOM	3875	CG	TYR	610	39.274	32.974	77.820	1.00	2.00	0
ATOM	3876	CD1	TYR	610	39.685	34.202	77.315	1.00	2.00	0
ATOM	3877	CE1	TYR	610	38.952	35.359	77.558	1.00	2.00	0

ATOM	3878	CD2	TYR	610	38.108	32.933	78.589	1.00	2.00	0
ATOM	3879	CE2	TYR	610	37.367	34.091	78.841	1.00	2.00	0
ATOM	3880	CZ	TYR	610	37.797	35.298	78.319	1.00	2.00	0
ATOM	3881	OH	TYR	610	37.086	36.452	78.533	1.00	2.00	0
ATOM	3883	C	TYR	610	40.431	29.342	78.205	1.00	2.00	0
ATOM	3884	O	TYR	610	39.481	28.575	78.006	1.00	2.00	0
ATOM	3885	N	LYS	611	41.703	28.991	78.017	1.00	2.00	0
ATOM	3887	CA	LYS	611	42.063	27.648	77.600	1.00	2.00	0
ATOM	3888	CB	LYS	611	43.551	27.532	77.308	1.00	3.53	0
ATOM	3889	CG	LYS	611	43.926	26.136	76.803	1.00	3.53	0
ATOM	3890	CD	LYS	611	43.240	25.837	75.467	1.00	3.53	0
ATOM	3891	CE	LYS	611	43.476	24.412	74.980	1.00	3.53	0
ATOM	3892	NZ	LYS	611	42.391	23.502	75.421	1.00	3.53	0
ATOM	3896	C	LYS	611	41.717	26.666	78.700	1.00	2.00	0
ATOM	3897	O	LYS	611	41.142	25.618	78.431	1.00	3.53	0
ATOM	3898	N	ILE	612	42.084	26.990	79.938	1.00	26.02	0
ATOM	3900	CA	ILE	612	41.780	26.115	81.069	1.00	26.02	0
ATOM	3901	CB	ILE	612	42.543	26.535	82.336	1.00	2.00	0
ATOM	3902	CG2	ILE	612	42.232	25.576	83.475	1.00	2.00	0
ATOM	3903	CG1	ILE	612	44.041	26.511	82.063	1.00	2.00	0
ATOM	3904	CD1	ILE	612	44.860	27.144	83.135	1.00	2.00	0
ATOM	3905	C	ILE	612	40.284	26.149	81.365	1.00	26.02	0
ATOM	3906	O	ILE	612	39.698	25.131	81.739	1.00	2.00	0
ATOM	3907	N	LYS	613	39.683	27.326	81.181	1.00	2.00	0
ATOM	3909	CA	LYS	613	38.257	27.556	81.414	1.00	2.00	0
ATOM	3910	CB	LYS	613	37.966	29.058	81.402	1.00	10.53	0
ATOM	3911	CG	LYS	613	36.528	29.437	81.650	1.00	10.53	0
ATOM	3912	CD	LYS	613	36.070	29.072	83.035	1.00	10.53	0
ATOM	3913	CE	LYS	613	34.717	29.693	83.364	1.00	10.53	0
ATOM	3914	NZ	LYS	613	33.611	29.182	82.523	1.00	10.53	0
ATOM	3918	C	LYS	613	37.379	26.847	80.384	1.00	2.00	0
ATOM	3919	O	LYS	613	36.335	26.293	80.739	1.00	10.53	0
ATOM	3920	N	TYR	614	37.819	26.842	79.121	1.00	24.09	0
ATOM	3922	CA	TYR	614	37.079	26.214	78.016	1.00	27.84	0
ATOM	3923	CB	TYR	614	36.473	27.301	77.125	1.00	2.00	0
ATOM	3924	CG	TYR	614	35.679	28.363	77.855	1.00	2.00	0
ATOM	3925	CD1	TYR	614	36.123	29.689	77.892	1.00	2.00	0
ATOM	3926	CE1	TYR	614	35.409	30.671	78.567	1.00	2.00	0
ATOM	3927	CD2	TYR	614	34.490	28.048	78.516	1.00	2.00	0
ATOM	3928	CE2	TYR	614	33.766	29.020	79.199	1.00	2.00	0
ATOM	3929	CZ	TYR	614	34.232	30.330	79.227	1.00	2.00	0
ATOM	3930	OH	TYR	614	33.560	31.293	79.960	1.00	2.00	0
ATOM	3932	C	TYR	614	37.976	25.317	77.146	1.00	25.93	0
ATOM	3933	O	TYR	614	38.012	25.474	75.935	1.00	2.00	0
ATOM	3934	N	PRO	615	38.641	24.310	77.733	1.00	21.49	0
ATOM	3935	CD	PRO	615	38.494	23.854	79.123	1.00	11.83	0
ATOM	3936	CA	PRO	615	39.541	23.406	76.995	1.00	22.47	0
ATOM	3937	CB	PRO	615	39.950	22.384	78.055	1.00	11.83	0
ATOM	3938	CG	PRO	615	38.773	22.382	78.995	1.00	11.83	0
ATOM	3939	C	PRO	615	39.078	22.714	75.720	1.00	20.23	0
ATOM	3940	O	PRO	615	39.873	22.026	75.074	1.00	11.83	0
ATOM	3941	N	GLU	616	37.813	22.879	75.350	1.00	15.62	0
ATOM	3943	CA	GLU	616	37.296	22.213	74.159	1.00	16.61	0
ATOM	3944	CB	GLU	616	36.240	21.179	74.566	1.00	26.75	0
ATOM	3945	CG	GLU	616	36.644	20.253	75.695	1.00	30.68	0
ATOM	3946	CD	GLU	616	37.872	19.416	75.382	1.00	40.71	0
ATOM	3947	OE1	GLU	616	38.747	19.294	76.273	1.00	39.65	0
ATOM	3948	OE2	GLU	616	37.960	18.874	74.256	1.00	39.29	0
ATOM	3949	C	GLU	616	36.681	23.175	73.140	1.00	13.01	0
ATOM	3950	O	GLU	616	36.276	22.765	72.046	1.00	20.06	0
ATOM	3951	N	ASN	617	36.620	24.453	73.499	1.00	2.00	0
ATOM	3953	CA	ASN	617	36.027	25.467	72.636	1.00	2.00	0
ATOM	3954	CB	ASN	617	34.678	25.896	73.218	1.00	42.63	0
ATOM	3955	CG	ASN	617	33.743	24.720	73.456	1.00	47.29	0
ATOM	3956	OD1	ASN	617	33.800	24.064	74.500	1.00	50.83	0
ATOM	3957	ND2	ASN	617	32.883	24.443	72.485	1.00	53.65	0
ATOM	3960	C	ASN	617	36.941	26.686	72.476	1.00	2.00	0
ATOM	3961	O	ASN	617	36.505	27.747	72.032	1.00	45.01	0

ATOM	3962	N	PHE	618	38.215	26.517	72.812	1.00	14.67	0
ATOM	3964	CA	PHE	618	39.192	27.596	72.736	1.00	14.67	0
ATOM	3965	CB	PHE	618	39.146	28.387	74.044	1.00	2.00	0
ATOM	3966	CG	PHE	618	40.042	29.585	74.073	1.00	2.00	0
ATOM	3967	CD1	PHE	618	39.501	30.871	74.058	1.00	2.00	0
ATOM	3968	CD2	PHE	618	41.422	29.441	74.147	1.00	2.00	0
ATOM	3969	CE1	PHE	618	40.322	32.007	74.119	1.00	2.00	0
ATOM	3970	CE2	PHE	618	42.254	30.562	74.209	1.00	2.00	0
ATOM	3971	CZ	PHE	618	41.696	31.854	74.195	1.00	2.00	0
ATOM	3972	C	PHE	618	40.540	26.907	72.570	1.00	14.67	0
ATOM	3973	O	PHE	618	40.893	26.066	73.394	1.00	2.00	0
ATOM	3974	N	PHE	619	41.285	27.239	71.514	1.00	2.00	0
ATOM	3976	CA	PHE	619	42.583	26.599	71.271	1.00	2.00	0
ATOM	3977	CB	PHE	619	42.468	25.622	70.111	1.00	2.00	0
ATOM	3978	CG	PHE	619	41.404	24.595	70.311	1.00	2.00	0
ATOM	3979	CD1	PHE	619	40.063	24.936	70.159	1.00	2.00	0
ATOM	3980	CD2	PHE	619	41.738	23.291	70.678	1.00	2.00	0
ATOM	3981	CE1	PHE	619	39.068	23.997	70.370	1.00	2.00	0
ATOM	3982	CE2	PHE	619	40.750	22.337	70.892	1.00	2.00	0
ATOM	3983	CZ	PHE	619	39.408	22.689	70.738	1.00	2.00	0
ATOM	3984	C	PHE	619	43.719	27.566	71.005	1.00	2.00	0
ATOM	3985	O	PHE	619	43.501	28.698	70.564	1.00	2.00	0
ATOM	3986	N	LEU	620	44.936	27.115	71.282	1.00	2.00	0
ATOM	3988	CA	LEU	620	46.118	27.933	71.073	1.00	2.00	0
ATOM	3989	CB	LEU	620	46.647	28.507	72.393	1.00	2.00	0
ATOM	3990	CG	LEU	620	45.826	29.389	73.321	1.00	2.00	0
ATOM	3991	CD1	LEU	620	46.741	29.868	74.437	1.00	2.00	0
ATOM	3992	CD2	LEU	620	45.247	30.563	72.565	1.00	2.00	0
ATOM	3993	C	LEU	620	47.225	27.093	70.438	1.00	2.00	0
ATOM	3994	O	LEU	620	47.548	25.987	70.910	1.00	2.00	0
ATOM	3995	N	LEU	621	47.805	27.634	69.376	1.00	2.00	0
ATOM	3997	CA	LEU	621	48.880	26.971	68.669	1.00	2.00	0
ATOM	3998	CB	LEU	621	48.577	26.929	67.162	1.00	2.00	0
ATOM	3999	CG	LEU	621	47.256	26.280	66.739	1.00	2.00	0
ATOM	4000	CD1	LEU	621	47.021	26.511	65.253	1.00	2.00	0
ATOM	4001	CD2	LEU	621	47.281	24.813	67.062	1.00	2.00	0
ATOM	4002	C	LEU	621	50.162	27.756	68.943	1.00	2.00	0
ATOM	4003	O	LEU	621	50.121	28.937	69.285	1.00	2.00	0
ATOM	4004	N	ARG	622	51.296	27.092	68.774	1.00	2.00	0
ATOM	4006	CA	ARG	622	52.593	27.690	69.013	1.00	2.00	0
ATOM	4007	CB	ARG	622	53.620	26.578	69.231	1.00	5.18	0
ATOM	4008	CG	ARG	622	54.967	27.052	69.716	1.00	5.18	0
ATOM	4009	CD	ARG	622	55.802	25.891	70.196	1.00	5.18	0
ATOM	4010	NE	ARG	622	56.969	26.357	70.941	1.00	5.18	0
ATOM	4012	CZ	ARG	622	57.830	25.553	71.557	1.00	5.18	0
ATOM	4013	NH1	ARG	622	57.659	24.240	71.525	1.00	6.18	0
ATOM	4016	NH2	ARG	622	58.870	26.056	72.199	1.00	5.18	0
ATOM	4019	C	ARG	622	53.070	28.615	67.894	1.00	2.00	0
ATOM	4020	O	ARG	622	53.032	28.270	66.702	1.00	16.40	0
ATOM	4021	N	GLY	623	53.508	29.805	68.286	1.00	19.04	0
ATOM	4023	CA	GLY	623	54.043	30.749	67.328	1.00	20.78	0
ATOM	4024	C	GLY	623	55.551	30.573	67.390	1.00	18.09	0
ATOM	4025	O	GLY	623	56.069	29.805	68.212	1.00	2.00	0
ATOM	4026	N	ASN	624	56.281	31.266	66.530	1.00	32.06	0
ATOM	4028	CA	ASN	624	57.728	31.144	66.566	1.00	32.95	0
ATOM	4029	CB	ASN	624	58.345	31.543	65.220	1.00	12.63	0
ATOM	4030	CG	ASN	624	58.120	33.002	64.857	1.00	8.84	0
ATOM	4031	OD1	ASN	624	57.381	33.754	65.538	1.00	9.47	0
ATOM	4032	ND2	ASN	624	58.721	33.411	63.757	1.00	8.50	0
ATOM	4035	C	ASN	624	58.260	31.988	67.721	1.00	32.42	0
ATOM	4036	O	ASN	624	59.442	31.926	68.066	1.00	7.81	0
ATOM	4037	N	HIS	625	57.359	32.757	68.335	1.00	7.73	0
ATOM	4039	CA	HIS	625	57.687	33.614	69.477	1.00	8.83	0
ATOM	4040	CB	HIS	625	57.030	34.987	69.320	1.00	2.00	0
ATOM	4041	CG	HIS	625	57.909	35.998	68.656	1.00	2.00	0
ATOM	4042	CD2	HIS	625	59.042	35.854	67.933	1.00	2.00	0
ATOM	4043	ND1	HIS	625	57.668	37.351	68.721	1.00	2.00	0
ATOM	4045	CE1	HIS	625	58.618	37.999	68.069	1.00	2.00	0

ATOM	4046	NE2	HIS	625	59.464	37.113	67.582	1.00	2.00	0
ATOM	4048	C	HIS	625	57.278	32.980	70.807	1.00	8.94	0
ATOM	4049	O	HIS	625	57.188	33.644	71.825	1.00	2.00	0
ATOM	4050	N	GLU	626	56.984	31.691	70.767	1.00	2.00	0
ATOM	4052	CA	GLU	626	56.629	30.914	71.945	1.00	2.00	0
ATOM	4053	CB	GLU	626	55.404	30.026	71.666	1.00	23.06	0
ATOM	4054	CG	GLU	626	54.051	30.627	72.039	1.00	18.70	0
ATOM	4055	CD	GLU	626	53.812	31.997	71.445	1.00	17.00	0
ATOM	4056	OE1	GLU	626	53.516	32.922	72.217	1.00	20.31	0
ATOM	4057	OE2	GLU	626	53.911	32.165	70.214	1.00	23.26	0
ATOM	4058	C	GLU	626	57.888	30.068	72.029	1.00	2.00	0
ATOM	4059	O	GLU	626	57.851	28.841	71.921	1.00	23.50	0
ATOM	4060	N	CYS	627	59.015	30.748	72.184	1.00	2.00	0
ATOM	4062	CA	CYS	627	60.290	30.067	72.218	1.00	2.00	0
ATOM	4063	CB	CYS	627	60.832	29.957	70.789	1.00	7.85	0
ATOM	4064	SG	CYS	627	62.235	28.843	70.575	1.00	19.90	0
ATOM	4065	C	CYS	627	61.260	30.842	73.105	1.00	2.00	0
ATOM	4066	O	CYS	627	61.355	32.066	73.008	1.00	8.12	0
ATOM	4067	N	ALA	628	61.971	30.116	73.970	1.00	19.49	0
ATOM	4069	CA	ALA	628	62.934	30.702	74.900	1.00	19.49	0
ATOM	4070	CB	ALA	628	63.704	29.601	75.567	1.00	2.00	0
ATOM	4071	C	ALA	628	63.890	31.662	74.206	1.00	19.49	0
ATOM	4072	O	ALA	628	63.921	32.859	74.484	1.00	2.00	0
ATOM	4073	N	SER	629	64.660	31.101	73.291	1.00	10.83	0
ATOM	4075	CA	SER	629	65.637	31.813	72.478	1.00	14.60	0
ATOM	4076	CB	SER	629	66.057	30.877	71.355	1.00	15.99	0
ATOM	4077	OG	SER	629	65.846	29.522	71.762	1.00	20.43	0
ATOM	4079	C	SER	629	65.119	33.131	71.899	1.00	19.16	0
ATOM	4080	O	SER	629	65.869	34.085	71.759	1.00	13.43	0
ATOM	4081	N	ILE	630	63.834	33.167	71.566	1.00	2.00	0
ATOM	4083	CA	ILE	630	63.198	34.354	71.022	1.00	2.00	0
ATOM	4084	CB	ILE	630	62.076	33.973	70.017	1.00	2.00	0
ATOM	4085	CG2	ILE	630	61.675	35.174	69.202	1.00	2.00	0
ATOM	4086	CG1	ILE	630	62.604	32.998	68.980	1.00	2.00	0
ATOM	4087	CD1	ILE	630	63.664	33.598	68.080	1.00	2.00	0
ATOM	4088	C	ILE	630	62.636	35.281	72.131	1.00	2.00	0
ATOM	4089	O	ILE	630	62.866	36.492	72.068	1.00	2.00	0
ATOM	4090	N	ASN	631	61.932	34.729	73.137	1.00	10.29	0
ATOM	4092	CA	ASN	631	61.350	35.504	74.272	1.00	9.61	0
ATOM	4093	CB	ASN	631	60.759	34.597	75.349	1.00	8.67	0
ATOM	4094	CG	ASN	631	59.555	33.848	74.891	1.00	17.37	0
ATOM	4095	OD1	ASN	631	59.189	33.896	73.722	1.00	21.10	0
ATOM	4096	ND2	ASN	631	58.926	33.124	75.815	1.00	15.25	0
ATOM	4099	C	ASN	631	62.367	36.370	75.003	1.00	6.75	0
ATOM	4100	O	ASN	631	62.059	37.486	75.438	1.00	6.80	0
ATOM	4101	N	ARG	632	63.555	35.810	75.189	1.00	2.00	0
ATOM	4103	CA	ARG	632	64.635	36.492	75.867	1.00	2.00	0
ATOM	4104	CB	ARG	632	65.873	35.595	75.909	1.00	6.06	0
ATOM	4105	CG	ARG	632	66.361	35.244	77.316	1.00	8.20	0
ATOM	4106	CD	ARG	632	67.436	36.202	77.839	1.00	8.31	0
ATOM	4107	NE	ARG	632	67.003	37.598	77.918	1.00	11.75	0
ATOM	4109	CZ	ARG	632	67.837	38.635	77.907	1.00	13.36	0
ATOM	4110	NH1	ARG	632	69.144	38.423	77.811	1.00	13.50	0
ATOM	4113	NH2	ARG	632	67.372	39.883	78.001	1.00	18.51	0
ATOM	4116	C	ARG	632	64.962	37.781	75.148	1.00	2.00	0
ATOM	4117	O	ARG	632	64.930	38.865	75.745	1.00	12.49	0
ATOM	4118	N	ILE	633	65.234	37.658	73.852	1.00	21.20	0
ATOM	4120	CA	ILE	633	65.608	38.788	73.014	1.00	19.86	0
ATOM	4121	CB	ILE	633	66.085	38.308	71.610	1.00	32.61	0
ATOM	4122	CG2	ILE	633	66.132	39.471	70.625	1.00	29.80	0
ATOM	4123	CG1	ILE	633	67.490	37.716	71.700	1.00	28.84	0
ATOM	4124	CD1	ILE	633	67.619	36.496	72.594	1.00	35.23	0
ATOM	4125	C	ILE	633	64.550	39.866	72.815	1.00	22.19	0
ATOM	4126	O	ILE	633	64.864	41.053	72.878	1.00	30.44	0
ATOM	4127	N	TYR	634	63.303	39.473	72.588	1.00	32.62	0
ATOM	4129	CA	TYR	634	62.276	40.471	72.316	1.00	31.19	0
ATOM	4130	CB	TYR	634	61.395	40.006	71.147	1.00	13.98	0
ATOM	4131	CG	TYR	634	62.231	39.755	69.941	1.00	19.07	0

ATOM	4132	CD1	TYR	634	62.652	40.805	69.147	1.00	17.28	0
ATOM	4133	CE1	TYR	634	63.498	40.587	68.074	1.00	16.13	0
ATOM	4134	CD2	TYR	634	62.668	38.474	69.639	1.00	15.20	0
ATOM	4135	CE2	TYR	634	63.515	38.236	68.571	1.00	18.14	0
ATOM	4136	CZ	TYR	634	63.935	39.296	67.786	1.00	21.41	0
ATOM	4137	OH	TYR	634	64.789	39.069	66.720	1.00	20.11	0
ATOM	4139	C	TYR	634	61.430	41.025	73.446	1.00	28.63	0
ATOM	4140	O	TYR	634	60.380	41.637	73.188	1.00	19.20	0
ATOM	4141	N	GLY	635	61.851	40.807	74.690	1.00	38.67	0
ATOM	4143	CA	GLY	635	61.114	41.407	75.786	1.00	39.39	0
ATOM	4144	C	GLY	635	60.270	40.658	76.780	1.00	41.31	0
ATOM	4145	O	GLY	635	60.103	41.155	77.892	1.00	69.69	0
ATOM	4146	N	PHE	636	59.725	39.502	76.431	1.00	54.49	0
ATOM	4148	CA	PHE	636	58.905	38.786	77.404	1.00	56.26	0
ATOM	4149	CB	PHE	636	58.386	37.461	76.831	1.00	2.00	0
ATOM	4150	CG	PHE	636	57.275	36.845	77.639	1.00	2.00	0
ATOM	4151	CD1	PHE	636	56.293	37.638	78.208	1.00	2.00	0
ATOM	4152	CD2	PHE	636	57.214	35.478	77.824	1.00	2.00	0
ATOM	4153	CE1	PHE	636	55.276	37.076	78.942	1.00	2.00	0
ATOM	4154	CE2	PHE	636	56.210	34.919	78.549	1.00	2.00	0
ATOM	4155	CZ	PHE	636	55.238	35.716	79.111	1.00	2.00	0
ATOM	4156	C	PHE	636	59.761	38.522	78.646	1.00	55.84	0
ATOM	4157	O	PHE	636	59.321	38.728	79.791	1.00	2.00	0
ATOM	4158	N	TYR	637	61.005	38.114	78.415	1.00	2.00	0
ATOM	4160	CA	TYR	637	61.918	37.836	79.506	1.00	2.00	0
ATOM	4161	CB	TYR	637	63.266	37.419	78.947	1.00	18.03	0
ATOM	4162	CG	TYR	637	64.345	37.308	79.986	1.00	13.39	0
ATOM	4163	CD1	TYR	637	64.560	36.116	80.668	1.00	15.45	0
ATOM	4164	CE1	TYR	637	65.563	36.007	81.603	1.00	14.13	0
ATOM	4165	CD2	TYR	637	65.163	38.390	80.273	1.00	14.83	0
ATOM	4166	CE2	TYR	637	66.163	38.292	81.200	1.00	13.98	0
ATOM	4167	CZ	TYR	637	66.363	37.101	81.863	1.00	14.88	0
ATOM	4168	OH	TYR	637	67.379	37.015	82.784	1.00	13.10	0
ATOM	4170	C	TYR	637	62.091	39.056	80.411	1.00	2.00	0
ATOM	4171	O	TYR	637	62.362	38.920	81.605	1.00	20.03	0
ATOM	4172	N	ASP	638	61.919	40.240	79.833	1.00	2.00	0
ATOM	4174	CA	ASP	638	62.086	41.484	80.554	1.00	2.00	0
ATOM	4175	CB	ASP	638	62.701	42.522	79.614	1.00	57.25	0
ATOM	4176	CG	ASP	638	64.049	42.053	79.046	1.00	66.80	0
ATOM	4177	OD1	ASP	638	64.078	41.539	77.905	1.00	65.06	0
ATOM	4178	OD2	ASP	638	65.077	42.175	79.750	1.00	69.12	0
ATOM	4179	C	ASP	638	60.816	41.961	81.245	1.00	2.00	0
ATOM	4180	O	ASP	638	60.884	42.531	82.331	1.00	55.83	0
ATOM	4181	N	GLU	639	59.656	41.724	80.644	1.00	2.00	0
ATOM	4183	CA	GLU	639	58.405	42.074	81.317	1.00	2.00	0
ATOM	4184	CB	GLU	639	57.210	41.774	80.419	1.00	64.74	0
ATOM	4185	CG	GLU	639	57.051	42.726	79.261	1.00	71.70	0
ATOM	4186	CD	GLU	639	55.900	42.349	78.355	1.00	66.55	0
ATOM	4187	OE1	GLU	639	54.748	42.718	78.667	1.00	65.31	0
ATOM	4188	OE2	GLU	639	56.152	41.684	77.329	1.00	72.66	0
ATOM	4189	C	GLU	639	58.372	41.145	82.547	1.00	2.00	0
ATOM	4190	O	GLU	639	58.009	41.550	83.654	1.00	65.95	0
ATOM	4191	N	CYS	640	58.787	39.895	82.314	1.00	15.74	0
ATOM	4193	CA	CYS	640	58.859	38.843	83.323	1.00	15.74	0
ATOM	4194	CB	CYS	640	59.187	37.504	82.684	1.00	4.35	0
ATOM	4195	SG	CYS	640	57.734	36.587	82.208	1.00	13.44	0
ATOM	4196	C	CYS	640	59.859	39.081	84.426	1.00	15.74	0
ATOM	4197	O	CYS	640	59.590	38.723	85.564	1.00	11.73	0
ATOM	4198	N	LYS	641	61.028	39.631	84.110	1.00	2.00	0
ATOM	4200	CA	LYS	641	62.009	39.890	85.153	1.00	2.00	0
ATOM	4201	CB	LYS	641	63.425	39.454	84.721	1.00	32.33	0
ATOM	4202	CG	LYS	641	64.225	40.436	83.869	1.00	32.55	0
ATOM	4203	CD	LYS	641	65.735	40.154	83.954	1.00	38.99	0
ATOM	4204	CE	LYS	641	66.281	40.198	85.386	1.00	41.14	0
ATOM	4205	NZ	LYS	641	66.228	41.554	86.007	1.00	38.23	0
ATOM	4209	C	LYS	641	61.950	41.371	85.568	1.00	2.00	0
ATOM	4210	O	LYS	641	62.948	42.106	85.548	1.00	35.25	0
ATOM	4211	N	ARG	642	60.750	41.801	85.945	1.00	17.38	0

ATOM	4213	CA	ARG	642	60.502	43.168	86.384	1.00	17.38	0
ATOM	4214	CB	ARG	642	60.341	44.131	85.204	1.00	14.00	0
ATOM	4215	CG	ARG	642	61.636	44.613	84.561	1.00	23.15	0
ATOM	4216	CD	ARG	642	61.463	46.016	83.940	1.00	25.43	0
ATOM	4217	NE	ARG	642	60.488	46.077	82.846	1.00	33.87	0
ATOM	4219	CZ	ARG	642	60.816	46.208	81.560	1.00	39.98	0
ATOM	4220	NH1	ARG	642	62.097	46.291	81.199	1.00	44.40	0
ATOM	4223	NH2	ARG	642	59.867	46.253	80.631	1.00	41.77	0
ATOM	4226	C	ARG	642	59.200	43.098	87.126	1.00	17.38	0
ATOM	4227	O	ARG	642	59.114	43.455	88.288	1.00	26.01	0
ATOM	4228	N	ARG	643	58.180	42.630	86.427	1.00	11.54	0
ATOM	4230	CA	ARG	643	56.869	42.500	87.018	1.00	11.54	0
ATOM	4231	CB	ARG	643	55.804	42.392	85.924	1.00	8.38	0
ATOM	4232	CG	ARG	643	55.526	43.749	85.304	1.00	8.38	0
ATOM	4233	CD	ARG	643	54.377	43.745	84.341	1.00	8.38	0
ATOM	4234	NE	ARG	643	53.121	43.351	84.949	1.00	8.38	0
ATOM	4236	CZ	ARG	643	51.939	43.569	84.390	1.00	8.38	0
ATOM	4237	NH1	ARG	643	51.869	44.187	83.218	1.00	8.38	0
ATOM	4240	NH2	ARG	643	50.825	43.157	84.985	1.00	8.38	0
ATOM	4243	C	ARG	643	56.841	41.304	87.939	1.00	11.54	0
ATOM	4244	O	ARG	643	56.156	41.309	88.969	1.00	8.38	0
ATOM	4245	N	TYR	644	57.606	40.285	87.565	1.00	2.00	0
ATOM	4247	CA	TYR	644	57.703	39.052	88.333	1.00	2.00	0
ATOM	4248	CB	TYR	644	56.784	37.972	87.741	1.00	14.67	0
ATOM	4249	CG	TYR	644	55.338	38.378	87.740	1.00	14.67	0
ATOM	4250	CD1	TYR	644	54.695	38.723	86.554	1.00	14.67	0
ATOM	4251	CE1	TYR	644	53.359	39.140	86.548	1.00	14.67	0
ATOM	4252	CD2	TYR	644	54.617	38.453	88.922	1.00	14.67	0
ATOM	4253	CE2	TYR	644	53.289	38.866	88.929	1.00	14.67	0
ATOM	4254	CZ	TYR	644	52.665	39.209	87.739	1.00	14.67	0
ATOM	4255	OH	TYR	644	51.349	39.629	87.741	1.00	14.67	0
ATOM	4257	C	TYR	644	59.160	38.598	88.330	1.00	2.00	0
ATOM	4258	O	TYR	644	60.062	39.412	88.575	1.00	14.67	0
ATOM	4259	N	ASN	645	59.399	37.321	88.028	1.00	2.00	0
ATOM	4261	CA	ASN	645	60.753	36.794	88.021	1.00	2.00	0
ATOM	4262	CB	ASN	645	61.103	36.147	89.379	1.00	16.19	0
ATOM	4263	CG	ASN	645	60.081	35.097	89.846	1.00	16.19	0
ATOM	4264	OD1	ASN	645	59.466	34.378	89.054	1.00	16.19	0
ATOM	4265	ND2	ASN	645	59.916	35.009	91.150	1.00	16.19	0
ATOM	4268	C	ASN	645	61.051	35.809	86.927	1.00	2.00	0
ATOM	4269	O	ASN	645	60.156	35.217	86.333	1.00	16.19	0
ATOM	4270	N	ILE	646	62.342	35.648	86.678	1.00	2.00	0
ATOM	4272	CA	ILE	646	62.856	34.716	85.689	1.00	2.00	0
ATOM	4273	CB	ILE	646	64.390	34.593	85.830	1.00	2.81	0
ATOM	4274	CG2	ILE	646	64.917	33.316	85.196	1.00	2.59	0
ATOM	4275	CG1	ILE	646	65.054	35.814	85.221	1.00	2.59	0
ATOM	4276	CD1	ILE	646	66.492	35.955	85.666	1.00	8.72	0
ATOM	4277	C	ILE	646	62.214	33.339	85.886	1.00	2.00	0
ATOM	4278	O	ILE	646	61.875	32.675	84.915	1.00	6.42	0
ATOM	4279	N	LYS	647	62.031	32.918	87.137	1.00	2.00	0
ATOM	4281	CA	LYS	647	61.441	31.614	87.411	1.00	2.00	0
ATOM	4282	CB	LYS	647	61.347	31.387	88.920	1.00	79.29	0
ATOM	4283	CG	LYS	647	62.714	31.450	89.594	1.00	84.06	0
ATOM	4284	CD	LYS	647	63.727	30.622	88.804	1.00	88.57	0
ATOM	4285	CE	LYS	647	65.157	31.090	89.028	1.00	86.67	0
ATOM	4286	NZ	LYS	647	66.029	30.668	87.886	1.00	91.44	0
ATOM	4290	C	LYS	647	60.083	31.478	86.738	1.00	2.00	0
ATOM	4291	O	LYS	647	59.751	30.426	86.187	1.00	74.01	0
ATOM	4292	N	LEU	648	59.322	32.563	86.763	1.00	25.02	0
ATOM	4294	CA	LEU	648	58.012	32.599	86.136	1.00	23.81	0
ATOM	4295	CB	LEU	648	57.300	33.918	86.460	1.00	2.00	0
ATOM	4296	CG	LEU	648	55.802	33.929	86.178	1.00	2.00	0
ATOM	4297	CD1	LEU	648	55.145	32.777	86.951	1.00	2.00	0
ATOM	4298	CD2	LEU	648	55.206	35.262	86.574	1.00	2.00	0
ATOM	4299	C	LEU	648	58.245	32.495	84.637	1.00	28.16	0
ATOM	4300	O	LEU	648	57.562	31.751	83.934	1.00	2.00	0
ATOM	4301	N	TRP	649	59.227	33.243	84.151	1.00	42.46	0
ATOM	4303	CA	TRP	649	59.554	33.224	82.738	1.00	40.96	0

ATOM	4304	CB	TRP	649	60.719	34.161	82.465	1.00	11.77	0
ATOM	4305	CG	TRP	649	61.206	34.051	81.081	1.00	14.98	0
ATOM	4306	CD2	TRP	649	62.393	33.394	80.653	1.00	14.05	0
ATOM	4307	CE2	TRP	649	62.460	33.527	79.246	1.00	12.39	0
ATOM	4308	CE3	TRP	649	63.412	32.703	81.320	1.00	25.06	0
ATOM	4309	CD1	TRP	649	60.607	34.546	79.951	1.00	17.81	0
ATOM	4310	NE1	TRP	649	61.356	34.232	78.846	1.00	15.30	0
ATOM	4312	CZ2	TRP	649	63.510	32.995	78.495	1.00	13.58	0
ATOM	4313	CZ3	TRP	649	64.456	32.174	80.576	1.00	15.93	0
ATOM	4314	CH2	TRP	649	64.497	32.323	79.175	1.00	16.10	0
ATOM	4315	C	TRP	649	59.900	31.802	82.292	1.00	40.42	0
ATOM	4316	O	TRP	649	59.392	31.315	81.285	1.00	12.84	0
ATOM	4317	N	LYS	650	60.748	31.138	83.069	1.00	2.00	0
ATOM	4319	CA	LYS	650	61.179	29.776	82.796	1.00	2.00	0
ATOM	4320	CB	LYS	650	62.257	29.371	83.795	1.00	19.18	0
ATOM	4321	CG	LYS	650	63.420	30.343	83.820	1.00	4.52	0
ATOM	4322	CD	LYS	650	64.541	29.898	84.718	1.00	3.83	0
ATOM	4323	CE	LYS	650	65.148	28.593	84.221	1.00	11.09	0
ATOM	4324	NZ	LYS	650	66.096	27.974	85.202	1.00	11.03	0
ATOM	4328	C	LYS	650	59.976	28.851	82.892	1.00	2.00	0
ATOM	4329	O	LYS	650	59.926	27.805	82.239	1.00	5.16	0
ATOM	4330	N	THR	651	58.997	29.234	83.702	1.00	10.53	0
ATOM	4332	CA	THR	651	57.792	28.422	83.838	1.00	14.10	0
ATOM	4333	CB	THR	651	56.915	28.882	85.038	1.00	23.55	0
ATOM	4334	OG1	THR	651	57.613	28.622	86.268	1.00	23.26	0
ATOM	4336	CG2	THR	651	55.582	28.150	85.047	1.00	24.53	0
ATOM	4337	C	THR	651	57.012	28.543	82.539	1.00	14.03	0
ATOM	4338	O	THR	651	56.599	27.534	81.951	1.00	23.01	0
ATOM	4339	N	PHE	652	56.837	29.779	82.082	1.00	2.00	0
ATOM	4341	CA	PHE	652	56.127	30.032	80.840	1.00	2.00	0
ATOM	4342	CB	PHE	652	56.225	31.511	80.440	1.00	2.00	0
ATOM	4343	CG	PHE	652	55.027	32.320	80.821	1.00	2.00	0
ATOM	4344	CD1	PHE	652	55.164	33.486	81.536	1.00	2.00	0
ATOM	4345	CD2	PHE	652	53.753	31.919	80.459	1.00	2.00	0
ATOM	4346	CE1	PHE	652	54.039	34.245	81.884	1.00	2.00	0
ATOM	4347	CE2	PHE	652	52.630	32.678	80.808	1.00	2.00	0
ATOM	4348	CZ	PHE	652	52.775	33.832	81.515	1.00	2.00	0
ATOM	4349	C	PHE	652	56.717	29.160	79.743	1.00	2.00	0
ATOM	4350	O	PHE	652	55.981	28.456	79.067	1.00	2.00	0
ATOM	4351	N	THR	653	58.039	29.143	79.608	1.00	2.00	0
ATOM	4353	CA	THR	653	58.631	28.344	78.552	1.00	2.00	0
ATOM	4354	CB	THR	653	60.126	28.538	78.429	1.00	2.14	0
ATOM	4355	OG1	THR	653	60.804	27.592	79.255	1.00	2.14	0
ATOM	4357	CG2	THR	653	60.499	29.945	78.787	1.00	2.14	0
ATOM	4358	C	THR	653	58.371	26.846	78.588	1.00	2.00	0
ATOM	4359	O	THR	653	58.452	26.196	77.555	1.00	4.20	0
ATOM	4360	N	ASP	654	58.064	26.271	79.743	1.00	2.00	0
ATOM	4362	CA	ASP	654	57.803	24.839	79.749	1.00	2.00	0
ATOM	4363	CB	ASP	654	58.083	24.225	81.119	1.00	25.83	0
ATOM	4364	CG	ASP	654	58.607	22.794	81.018	1.00	26.00	0
ATOM	4365	OD1	ASP	654	59.163	22.420	79.960	1.00	29.22	0
ATOM	4366	OD2	ASP	654	58.472	22.043	82.006	1.00	28.12	0
ATOM	4367	C	ASP	654	56.367	24.603	79.332	1.00	2.00	0
ATOM	4368	O	ASP	654	56.014	23.518	78.874	1.00	18.75	0
ATOM	4369	N	CYS	655	55.537	25.625	79.503	1.00	27.58	0
ATOM	4371	CA	CYS	655	54.146	25.546	79.095	1.00	27.58	0
ATOM	4372	CB	CYS	655	53.333	26.675	79.722	1.00	8.45	0
ATOM	4373	SG	CYS	655	51.756	26.978	78.901	1.00	8.45	0
ATOM	4374	C	CYS	655	54.162	25.683	77.575	1.00	27.58	0
ATOM	4375	O	CYS	655	53.565	24.863	76.865	1.00	8.45	0
ATOM	4376	N	PHE	656	54.871	26.709	77.088	1.00	7.64	0
ATOM	4378	CA	PHE	656	55.018	26.966	75.653	1.00	7.64	0
ATOM	4379	CB	PHE	656	55.967	28.145	75.402	1.00	12.44	0
ATOM	4380	CG	PHE	656	55.384	29.483	75.747	1.00	12.44	0
ATOM	4381	CD1	PHE	656	54.073	29.591	76.242	1.00	12.44	0
ATOM	4382	CD2	PHE	656	56.144	30.641	75.594	1.00	12.44	0
ATOM	4383	CE1	PHE	656	53.525	30.840	76.585	1.00	12.44	0
ATOM	4384	CE2	PHE	656	55.614	31.891	75.929	1.00	12.44	0

ATOM	4385	CZ	PHE	656	54.296	31.990	76.430	1.00	12.44	0
ATOM	4386	C	PHE	656	55.564	25.705	74.961	1.00	7.64	0
ATOM	4387	O	PHE	656	55.033	25.274	73.940	1.00	12.44	0
ATOM	4388	N	ASN	657	56.595	25.099	75.543	1.00	2.00	0
ATOM	4390	CA	ASN	657	57.198	23.896	75.006	1.00	2.00	0
ATOM	4391	CB	ASN	657	58.353	23.425	75.892	1.00	12.64	0
ATOM	4392	CG	ASN	657	59.614	24.233	75.690	1.00	12.64	0
ATOM	4393	OD1	ASN	657	59.564	25.404	75.350	1.00	12.64	0
ATOM	4394	ND2	ASN	657	60.757	23.607	75.896	1.00	12.64	0
ATOM	4397	C	ASN	657	56.202	22.772	74.881	1.00	2.00	0
ATOM	4398	O	ASN	657	56.585	21.668	74.532	1.00	12.64	0
ATOM	4399	N	CYS	658	54.934	23.017	75.196	1.00	2.00	0
ATOM	4401	CA	CYS	658	53.930	21.964	75.080	1.00	2.00	0
ATOM	4402	CB	CYS	658	53.543	21.468	76.475	1.00	10.87	0
ATOM	4403	SG	CYS	658	55.004	20.919	77.397	1.00	10.87	0
ATOM	4404	C	CYS	658	52.708	22.390	74.258	1.00	2.00	0
ATOM	4405	O	CYS	658	51.726	21.659	74.162	1.00	10.87	0
ATOM	4406	N	LEU	659	52.799	23.560	73.634	1.00	11.17	0
ATOM	4408	CA	LEU	659	51.739	24.085	72.781	1.00	11.17	0
ATOM	4409	CB	LEU	659	51.998	25.569	72.470	1.00	2.00	0
ATOM	4410	CG	LEU	659	51.757	26.629	73.542	1.00	2.00	0
ATOM	4411	CD1	LEU	659	52.286	27.965	73.123	1.00	2.00	0
ATOM	4412	CD2	LEU	659	50.307	26.759	73.767	1.00	2.00	0
ATOM	4413	C	LEU	659	51.651	23.298	71.450	1.00	11.17	0
ATOM	4414	O	LEU	659	52.681	22.845	70.900	1.00	2.00	0
ATOM	4415	N	PRO	660	50.415	23.109	70.931	1.00	14.96	0
ATOM	4416	CD	PRO	660	49.134	23.535	71.523	1.00	2.00	0
ATOM	4417	CA	PRO	660	50.166	22.398	69.680	1.00	14.96	0
ATOM	4418	CB	PRO	660	48.640	22.381	69.590	1.00	2.00	0
ATOM	4419	CG	PRO	660	48.194	22.472	71.028	1.00	2.00	0
ATOM	4420	C	PRO	660	50.796	23.248	68.579	1.00	14.96	0
ATOM	4421	O	PRO	660	50.888	24.474	68.709	1.00	2.00	0
ATOM	4422	N	ILE	661	51.195	22.603	67.488	1.00	28.66	0
ATOM	4424	CA	ILE	661	51.880	23.279	66.397	1.00	30.55	0
ATOM	4425	CB	ILE	661	53.126	22.480	66.036	1.00	19.83	0
ATOM	4426	CG2	ILE	661	54.064	22.432	67.228	1.00	22.82	0
ATOM	4427	CG1	ILE	661	52.728	21.050	65.669	1.00	24.89	0
ATOM	4428	CD1	ILE	661	53.896	20.161	65.299	1.00	29.65	0
ATOM	4429	C	ILE	661	51.074	23.577	65.132	1.00	29.24	0
ATOM	4430	O	ILE	661	51.428	24.493	64.372	1.00	20.63	0
ATOM	4431	N	ALA	662	50.004	22.810	64.915	1.00	22.79	0
ATOM	4433	CA	ALA	662	49.112	22.970	63.751	1.00	22.79	0
ATOM	4434	CB	ALA	662	49.652	22.187	62.529	1.00	2.00	0
ATOM	4435	C	ALA	662	47.683	22.507	64.086	1.00	22.79	0
ATOM	4436	O	ALA	662	47.439	21.887	65.139	1.00	2.00	0
ATOM	4437	N	ALA	663	46.739	22.816	63.205	1.00	2.00	0
ATOM	4439	CA	ALA	663	45.347	22.438	63.410	1.00	2.00	0
ATOM	4440	CB	ALA	663	44.599	23.535	64.124	1.00	18.31	0
ATOM	4441	C	ALA	663	44.748	22.223	62.053	1.00	2.00	0
ATOM	4442	O	ALA	663	45.323	22.623	61.041	1.00	22.14	0
ATOM	4443	N	ILE	664	43.600	21.565	62.028	1.00	16.69	0
ATOM	4445	CA	ILE	664	42.892	21.300	60.788	1.00	16.69	0
ATOM	4446	CB	ILE	664	43.240	19.885	60.208	1.00	9.81	0
ATOM	4447	CG2	ILE	664	42.396	19.597	58.976	1.00	9.81	0
ATOM	4448	CG1	ILE	664	44.724	19.810	59.819	1.00	9.81	0
ATOM	4449	CD1	ILE	664	45.161	18.450	59.316	1.00	9.81	0
ATOM	4450	C	ILE	664	41.408	21.397	61.118	1.00	16.69	0
ATOM	4451	O	ILE	664	40.880	20.603	61.899	1.00	9.81	0
ATOM	4452	N	VAL	665	40.754	22.408	60.561	1.00	14.09	0
ATOM	4454	CA	VAL	665	39.332	22.608	60.777	1.00	14.09	0
ATOM	4455	CB	VAL	665	38.954	24.091	60.742	1.00	2.00	0
ATOM	4456	CG1	VAL	665	37.450	24.239	60.710	1.00	2.00	0
ATOM	4457	CG2	VAL	665	39.500	24.788	61.950	1.00	2.00	0
ATOM	4458	C	VAL	665	38.509	21.873	59.729	1.00	14.09	0
ATOM	4459	O	VAL	665	38.768	21.972	58.524	1.00	2.00	0
ATOM	4460	N	ASP	666	37.517	21.137	60.219	1.00	2.00	0
ATOM	4462	CA	ASP	666	36.595	20.345	59.407	1.00	2.00	0
ATOM	4463	CB	ASP	666	35.443	21.235	58.933	1.00	65.64	0

ATOM	4464	CG	ASP	666	34.545	21.675	60.081	1.00	73.26	0
ATOM	4465	OD1	ASP	666	33.763	20.838	60.578	1.00	71.65	0
ATOM	4466	OD2	ASP	666	34.623	22.851	60.493	1.00	75.52	0
ATOM	4467	C	ASP	666	37.234	19.577	58.235	1.00	2.00	0
ATOM	4468	O	ASP	666	36.648	19.467	57.158	1.00	57.66	0
ATOM	4469	N	GLU	667	38.439	19.048	58.472	1.00	17.20	0
ATOM	4471	CA	GLU	667	39.203	18.270	57.489	1.00	17.69	0
ATOM	4472	CB	GLU	667	38.455	16.981	57.138	1.00	42.87	0
ATOM	4473	CG	GLU	667	38.170	16.101	58.345	1.00	52.20	0
ATOM	4474	CD	GLU	667	37.457	14.806	57.988	1.00	53.85	0
ATOM	4475	OE1	GLU	667	36.222	14.717	58.211	1.00	51.15	0
ATOM	4476	OE2	GLU	667	38.139	13.877	57.494	1.00	55.67	0
ATOM	4477	C	GLU	667	39.584	19.015	56.207	1.00	17.24	0
ATOM	4478	O	GLU	667	40.146	18.421	55.286	1.00	34.30	0
ATOM	4479	N	LYS	668	39.314	20.319	56.172	1.00	26.53	0
ATOM	4481	CA	LYS	668	39.615	21.133	55.002	1.00	20.22	0
ATOM	4482	CB	LYS	668	38.318	21.709	54.410	1.00	13.48	0
ATOM	4483	CG	LYS	668	37.383	20.628	53.859	1.00	13.48	0
ATOM	4484	CD	LYS	668	38.119	19.779	52.819	1.00	13.48	0
ATOM	4485	CE	LYS	668	37.341	18.551	52.398	1.00	16.60	0
ATOM	4486	NZ	LYS	668	38.247	17.564	51.739	1.00	18.66	0
ATOM	4490	C	LYS	668	40.636	22.244	55.240	1.00	19.61	0
ATOM	4491	O	LYS	668	41.676	22.264	54.584	1.00	13.48	0
ATOM	4492	N	ILE	669	40.356	23.166	56.158	1.00	2.00	0
ATOM	4494	CA	ILE	669	41.295	24.263	56.424	1.00	2.00	0
ATOM	4495	CB	ILE	669	40.617	25.456	57.183	1.00	2.00	0
ATOM	4496	CG2	ILE	669	41.521	26.680	57.166	1.00	2.00	0
ATOM	4497	CG1	ILE	669	39.298	25.839	56.518	1.00	2.00	0
ATOM	4498	CD1	ILE	669	38.581	26.960	57.189	1.00	2.00	0
ATOM	4499	C	ILE	669	42.439	23.721	57.279	1.00	2.00	0
ATOM	4500	O	ILE	669	42.201	23.034	58.269	1.00	2.00	0
ATOM	4501	N	PHE	670	43.673	24.010	56.892	1.00	2.00	0
ATOM	4503	CA	PHE	670	44.841	23.551	57.641	1.00	2.00	0
ATOM	4504	CB	PHE	670	45.804	22.801	56.718	1.00	2.00	0
ATOM	4505	CG	PHE	670	47.182	22.614	57.291	1.00	2.00	0
ATOM	4506	CD1	PHE	670	47.503	21.473	58.007	1.00	2.00	0
ATOM	4507	CD2	PHE	670	48.163	23.569	57.093	1.00	2.00	0
ATOM	4508	CE1	PHE	670	48.769	21.288	58.506	1.00	2.00	0
ATOM	4509	CE2	PHE	670	49.436	23.384	57.596	1.00	2.00	0
ATOM	4510	CZ	PHE	670	49.737	22.241	58.302	1.00	2.00	0
ATOM	4511	C	PHE	670	45.528	24.780	58.190	1.00	2.00	0
ATOM	4512	O	PHE	670	45.901	25.652	57.421	1.00	2.00	0
ATOM	4513	N	CYS	671	45.725	24.839	59.501	1.00	2.00	0
ATOM	4515	CA	CYS	671	46.353	25.992	60.120	1.00	2.00	0
ATOM	4516	CB	CYS	671	45.395	26.596	61.136	1.00	14.45	0
ATOM	4517	SG	CYS	671	43.708	26.779	60.568	1.00	25.33	0
ATOM	4518	C	CYS	671	47.685	25.701	60.816	1.00	2.00	0
ATOM	4519	O	CYS	671	47.921	24.589	61.310	1.00	8.01	0
ATOM	4520	N	CYS	672	48.546	26.714	60.845	1.00	2.00	0
ATOM	4522	CA	CYS	672	49.845	26.666	61.515	1.00	2.00	0
ATOM	4523	CB	CYS	672	50.826	25.741	60.792	1.00	9.00	0
ATOM	4524	SG	CYS	672	51.494	26.372	59.265	1.00	11.24	0
ATOM	4525	C	CYS	672	50.336	28.122	61.525	1.00	2.00	0
ATOM	4526	O	CYS	672	49.751	28.963	60.850	1.00	9.00	0
ATOM	4527	N	HIS	673	51.369	28.440	62.300	1.00	17.94	0
ATOM	4529	CA	HIS	673	51.855	29.817	62.360	1.00	17.94	0
ATOM	4530	C	HIS	673	52.456	30.359	61.065	1.00	17.94	0
ATOM	4531	O	HIS	673	51.960	31.349	60.514	1.00	2.00	0
ATOM	4532	CB	HIS	673	52.894	29.965	63.459	1.00	2.00	0
ATOM	4533	CG	HIS	673	53.283	31.383	63.724	1.00	2.00	0
ATOM	4534	ND1	HIS	673	52.388	32.377	64.033	1.00	2.00	0
ATOM	4536	CD2	HIS	673	54.503	31.975	63.718	1.00	2.00	0
ATOM	4537	NE2	HIS	673	54.371	33.330	64.019	1.00	2.00	0
ATOM	4538	CE1	HIS	673	53.072	33.512	64.199	1.00	2.00	0
ATOM	4539	N	GLY	674	53.545	29.721	60.626	1.00	2.00	0
ATOM	4541	CA	GLY	674	54.260	30.101	59.417	1.00	2.00	0
ATOM	4542	C	GLY	674	53.773	29.407	58.163	1.00	2.00	0
ATOM	4543	O	GLY	674	53.410	30.063	57.203	1.00	11.62	0

ATOM	4544	N	GLY	675	53.759	28.087	58.136	1.00	6.25	0
ATOM	4546	CA	GLY	675	53.286	27.440	56.931	1.00	6.25	0
ATOM	4547	C	GLY	675	53.823	26.061	56.604	1.00	6.25	0
ATOM	4548	O	GLY	675	53.867	25.173	57.452	1.00	28.15	0
ATOM	4549	N	LEU	676	54.241	25.883	55.356	1.00	2.00	0
ATOM	4551	CA	LEU	676	54.723	24.591	54.886	1.00	2.00	0
ATOM	4552	CB	LEU	676	54.336	24.409	53.418	1.00	2.00	0
ATOM	4553	CG	LEU	676	52.827	24.625	53.244	1.00	2.00	0
ATOM	4554	CD1	LEU	676	52.412	24.556	51.777	1.00	2.00	0
ATOM	4555	CD2	LEU	676	52.100	23.575	54.075	1.00	2.00	0
ATOM	4556	C	LEU	676	56.207	24.333	55.095	1.00	2.00	0
ATOM	4557	O	LEU	676	56.981	25.248	55.381	1.00	2.00	0
ATOM	4558	N	SER	677	56.582	23.069	54.945	1.00	12.63	0
ATOM	4560	CA	SER	677	57.946	22.617	55.141	1.00	12.63	0
ATOM	4561	CB	SER	677	58.083	21.985	56.539	1.00	2.43	0
ATOM	4562	OG	SER	677	59.248	21.192	56.649	1.00	2.03	0
ATOM	4564	C	SER	677	58.247	21.556	54.095	1.00	12.63	0
ATOM	4565	O	SER	677	57.405	20.684	53.838	1.00	10.72	0
ATOM	4566	N	PRO	678	59.449	21.605	53.484	1.00	2.00	0
ATOM	4567	CD	PRO	678	60.474	22.638	53.681	1.00	15.59	0
ATOM	4568	CA	PRO	678	59.887	20.647	52.469	1.00	2.00	0
ATOM	4569	CB	PRO	678	61.329	21.076	52.184	1.00	15.59	0
ATOM	4570	CG	PRO	678	61.299	22.517	52.416	1.00	15.59	0
ATOM	4571	C	PRO	678	59.859	19.234	53.032	1.00	2.00	0
ATOM	4572	O	PRO	678	59.990	18.269	52.293	1.00	15.59	0
ATOM	4573	N	ASP	679	59.685	19.112	54.342	1.00	2.00	0
ATOM	4575	CA	ASP	679	59.687	17.813	54.992	1.00	2.00	0
ATOM	4576	CB	ASP	679	60.510	17.926	56.271	1.00	26.28	0
ATOM	4577	CG	ASP	679	61.766	18.758	56.073	1.00	24.05	0
ATOM	4578	OD1	ASP	679	62.687	18.269	55.383	1.00	32.92	0
ATOM	4579	OD2	ASP	679	61.826	19.902	56.586	1.00	28.53	0
ATOM	4580	C	ASP	679	58.303	17.278	55.314	1.00	2.00	0
ATOM	4581	O	ASP	679	58.129	16.094	55.576	1.00	24.04	0
ATOM	4582	N	LEU	680	57.315	18.149	55.279	1.00	2.00	0
ATOM	4584	CA	LEU	680	55.970	17.747	55.622	1.00	2.00	0
ATOM	4585	CB	LEU	680	55.147	19.000	55.916	1.00	4.45	0
ATOM	4586	CG	LEU	680	53.683	18.788	56.262	1.00	2.86	0
ATOM	4587	CD1	LEU	680	53.540	17.791	57.398	1.00	2.86	0
ATOM	4588	CD2	LEU	680	53.085	20.134	56.582	1.00	2.86	0
ATOM	4589	C	LEU	680	55.262	16.862	54.588	1.00	2.00	0
ATOM	4590	O	LEU	680	54.421	17.331	53.814	1.00	15.95	0
ATOM	4591	N	GLN	681	55.588	15.578	54.561	1.00	2.00	0
ATOM	4593	CA	GLN	681	54.922	14.686	53.611	1.00	2.00	0
ATOM	4594	CB	GLN	681	55.719	13.410	53.385	1.00	36.99	0
ATOM	4595	CG	GLN	681	57.097	13.620	52.863	1.00	36.99	0
ATOM	4596	CD	GLN	681	57.716	12.321	52.468	1.00	36.99	0
ATOM	4597	OE1	GLN	681	57.589	11.894	51.326	1.00	36.99	0
ATOM	4598	NE2	GLN	681	58.377	11.663	53.409	1.00	36.99	0
ATOM	4601	C	GLN	681	53.551	14.319	54.159	1.00	2.00	0
ATOM	4602	O	GLN	681	52.547	14.392	53.445	1.00	11.55	0
ATOM	4603	N	SER	682	53.505	13.923	55.423	1.00	39.00	0
ATOM	4605	CA	SER	682	52.238	13.566	56.027	1.00	42.03	0
ATOM	4606	CB	SER	682	52.131	12.048	56.224	1.00	2.00	0
ATOM	4607	OG	SER	682	53.198	11.507	56.993	1.00	2.00	0
ATOM	4609	C	SER	682	52.003	14.284	57.343	1.00	38.75	0
ATOM	4610	O	SER	682	52.941	14.742	58.009	1.00	2.00	0
ATOM	4611	N	MET	683	50.730	14.397	57.698	1.00	15.16	0
ATOM	4613	CA	MET	683	50.338	15.029	58.938	1.00	15.16	0
ATOM	4614	CB	MET	683	48.820	15.069	59.044	1.00	11.68	0
ATOM	4615	CG	MET	683	48.099	15.565	57.799	1.00	12.75	0
ATOM	4616	SD	MET	683	48.197	17.328	57.477	1.00	11.68	0
ATOM	4617	CE	MET	683	49.486	17.429	56.200	1.00	12.61	0
ATOM	4618	C	MET	683	50.906	14.131	60.024	1.00	15.16	0
ATOM	4619	O	MET	683	51.215	14.585	61.116	1.00	15.01	0
ATOM	4620	N	GLU	684	51.050	12.848	59.705	1.00	40.22	0
ATOM	4622	CA	GLU	684	51.597	11.881	60.644	1.00	41.85	0
ATOM	4623	CB	GLU	684	52.007	10.594	59.937	1.00	63.04	0
ATOM	4624	CG	GLU	684	52.850	9.689	60.823	1.00	72.94	0

ATOM	4625	CD	GLU	684	53.111	8.343	60.206	1.00	77.43	0
ATOM	4626	OE1	GLU	684	52.139	7.716	59.730	1.00	77.96	0
ATOM	4627	OE2	GLU	684	54.285	7.909	60.201	1.00	79.67	0
ATOM	4628	C	GLU	684	52.819	12.471	61.297	1.00	40.42	0
ATOM	4629	O	GLU	684	52.932	12.495	62.517	1.00	62.00	0
ATOM	4630	N	GLN	685	53.727	12.959	60.466	1.00	2.00	0
ATOM	4632	CA	GLN	685	54.945	13.559	60.952	1.00	2.00	0
ATOM	4633	CB	GLN	685	55.703	14.200	59.797	1.00	52.45	0
ATOM	4634	CG	GLN	685	56.162	13.188	58.775	1.00	57.01	0
ATOM	4635	CD	GLN	685	56.779	13.832	57.574	1.00	58.68	0
ATOM	4636	OE1	GLN	685	56.258	13.728	56.471	1.00	68.68	0
ATOM	4637	NE2	GLN	685	57.895	14.510	57.778	1.00	65.77	0
ATOM	4640	C	GLN	685	54.627	14.585	62.029	1.00	2.00	0
ATOM	4641	O	GLN	685	55.312	14.631	63.056	1.00	54.77	0
ATOM	4642	N	ILE	686	53.579	15.387	61.816	1.00	16.80	0
ATOM	4644	CA	ILE	686	53.179	16.391	62.807	1.00	14.42	0
ATOM	4645	CB	ILE	686	51.990	17.270	62.307	1.00	2.00	0
ATOM	4646	CG2	ILE	686	51.754	18.441	63.247	1.00	2.00	0
ATOM	4647	CG1	ILE	686	52.304	17.869	60.944	1.00	2.00	0
ATOM	4648	CD1	ILE	686	51.139	18.668	60.369	1.00	2.00	0
ATOM	4649	C	ILE	686	52.761	15.633	64.079	1.00	13.83	0
ATOM	4650	O	ILE	686	53.289	15.884	65.165	1.00	2.00	0
ATOM	4651	N	ARG	687	51.856	14.669	63.914	1.00	3.14	0
ATOM	4653	CA	ARG	687	51.367	13.855	65.027	1.00	3.14	0
ATOM	4654	CB	ARG	687	50.307	12.835	64.564	1.00	23.50	0
ATOM	4655	CG	ARG	687	49.266	13.324	63.559	1.00	26.96	0
ATOM	4656	CD	ARG	687	48.288	12.211	63.083	1.00	35.95	0
ATOM	4657	NE	ARG	687	48.878	11.199	62.190	1.00	41.22	0
ATOM	4659	CZ	ARG	687	49.583	10.138	62.594	1.00	45.24	0
ATOM	4660	NH1	ARG	687	50.062	9.283	61.702	1.00	43.65	0
ATOM	4663	NH2	ARG	687	49.827	9.922	63.887	1.00	36.26	0
ATOM	4666	C	ARG	687	52.504	13.060	65.665	1.00	3.14	0
ATOM	4667	O	ARG	687	52.260	12.327	66.613	1.00	18.08	0
ATOM	4668	N	ARG	688	53.722	13.157	65.136	1.00	11.08	0
ATOM	4670	CA	ARG	688	54.841	12.402	65.694	1.00	10.97	0
ATOM	4671	CB	ARG	688	55.576	11.624	64.595	1.00	52.72	0
ATOM	4672	CG	ARG	688	54.794	10.485	63.995	1.00	52.20	0
ATOM	4673	CD	ARG	688	54.421	9.463	65.035	1.00	55.85	0
ATOM	4674	NE	ARG	688	53.634	8.372	64.468	1.00	50.50	0
ATOM	4676	CZ	ARG	688	54.145	7.254	63.956	1.00	54.57	0
ATOM	4677	NH1	ARG	688	53.335	6.326	63.465	1.00	53.02	0
ATOM	4680	NH2	ARG	688	55.457	7.056	63.931	1.00	50.07	0
ATOM	4683	C	ARG	688	55.853	13.257	66.457	1.00	9.37	0
ATOM	4684	O	ARG	688	56.771	12.719	67.084	1.00	54.51	0
ATOM	4685	N	ILE	689	55.698	14.576	66.398	1.00	38.26	0
ATOM	4687	CA	ILE	689	56.614	15.487	67.081	1.00	36.62	0
ATOM	4688	CB	ILE	689	56.319	16.952	66.673	1.00	2.00	0
ATOM	4689	CG2	ILE	689	57.248	17.901	67.399	1.00	2.00	0
ATOM	4690	CG1	ILE	689	56.493	17.119	65.160	1.00	2.00	0
ATOM	4691	CD1	ILE	689	56.670	18.556	64.711	1.00	2.00	0
ATOM	4692	C	ILE	689	56.552	15.347	68.620	1.00	42.28	0
ATOM	4693	O	ILE	689	55.468	15.462	69.226	1.00	2.00	0
ATOM	4694	N	MET	690	57.710	15.084	69.242	1.00	2.00	0
ATOM	4696	CA	MET	690	57.794	14.930	70.704	1.00	2.00	0
ATOM	4697	CB	MET	690	59.204	14.516	71.138	1.00	31.54	0
ATOM	4698	CG	MET	690	59.657	13.160	70.616	1.00	36.54	0
ATOM	4699	SD	MET	690	58.703	11.742	71.207	1.00	43.14	0
ATOM	4700	CE	MET	690	59.784	10.411	70.721	1.00	40.70	0
ATOM	4701	C	MET	690	57.491	16.313	71.227	1.00	2.00	0
ATOM	4702	O	MET	690	58.189	17.269	70.864	1.00	21.20	0
ATOM	4703	N	ARG	691	56.489	16.441	72.092	1.00	59.62	0
ATOM	4705	CA	ARG	691	56.135	17.780	72.507	1.00	65.12	0
ATOM	4706	CB	ARG	691	54.678	17.879	72.869	1.00	2.00	0
ATOM	4707	CG	ARG	691	54.077	19.116	72.206	1.00	2.00	0
ATOM	4708	CD	ARG	691	52.598	19.166	72.384	1.00	2.00	0
ATOM	4709	NE	ARG	691	52.082	17.820	72.551	1.00	2.00	0
ATOM	4711	CZ	ARG	691	50.832	17.540	72.862	1.00	2.00	0
ATOM	4712	NH1	ARG	691	49.957	18.525	73.024	1.00	2.00	0

ATOM	4715	NH2	ARG	691	50.482	16.273	73.046	1.00	2.00	0
ATOM	4718	C	ARG	691	56.930	18.632	73.458	1.00	64.88	0
ATOM	4719	O	ARG	691	57.176	19.794	73.100	1.00	2.00	0
ATOM	4720	N	PRO	692	57.265	18.151	74.693	1.00	0.89	0
ATOM	4721	CD	PRO	692	56.930	16.947	75.482	1.00	19.88	0
ATOM	4722	CA	PRO	692	58.060	19.115	75.500	1.00	0.77	0
ATOM	4723	CB	PRO	692	58.305	18.357	76.811	1.00	21.87	0
ATOM	4724	CG	PRO	692	57.071	17.462	76.911	1.00	19.02	0
ATOM	4725	C	PRO	692	59.327	19.317	74.643	1.00	0.10	0
ATOM	4726	O	PRO	692	60.258	18.502	74.690	1.00	22.15	0
ATOM	4727	N	THR	693	59.310	20.362	73.811	1.00	2.00	0
ATOM	4729	CA	THR	693	60.395	20.605	72.896	1.00	2.00	0
ATOM	4730	CB	THR	693	60.153	19.842	71.569	1.00	39.91	0
ATOM	4731	OG1	THR	693	61.310	19.947	70.728	1.00	47.46	0
ATOM	4733	CG2	THR	693	58.944	20.419	70.830	1.00	46.31	0
ATOM	4734	C	THR	693	60.567	22.057	72.560	1.00	2.00	0
ATOM	4735	O	THR	693	59.640	22.848	72.678	1.00	41.07	0
ATOM	4736	N	ASP	694	61.782	22.399	72.154	1.00	4.51	0
ATOM	4738	CA	ASP	694	62.075	23.747	71.736	1.00	4.51	0
ATOM	4739	CB	ASP	694	63.429	24.203	72.283	1.00	83.74	0
ATOM	4740	CG	ASP	694	63.337	25.520	73.041	1.00	83.74	0
ATOM	4741	OD1	ASP	694	63.231	25.484	74.285	1.00	83.74	0
ATOM	4742	OD2	ASP	694	63.366	26.594	72.400	1.00	83.74	0
ATOM	4743	C	ASP	694	62.101	23.682	70.201	1.00	4.51	0
ATOM	4744	O	ASP	694	62.403	22.632	69.629	1.00	83.74	0
ATOM	4745	N	VAL	695	61.743	24.784	69.546	1.00	31.71	0
ATOM	4747	CA	VAL	695	61.760	24.864	68.087	1.00	37.86	0
ATOM	4748	CB	VAL	695	61.212	26.224	67.623	1.00	72.52	0
ATOM	4749	CG1	VAL	695	61.120	26.268	66.113	1.00	68.63	0
ATOM	4750	CG2	VAL	695	59.863	26.474	68.253	1.00	68.27	0
ATOM	4751	C	VAL	695	63.242	24.744	67.687	1.00	34.22	0
ATOM	4752	O	VAL	695	64.070	25.548	68.123	1.00	75.22	0
ATOM	4753	N	PRO	696	63.599	23.730	66.873	1.00	2.00	0
ATOM	4754	CD	PRO	696	62.777	22.616	66.373	1.00	5.25	0
ATOM	4755	CA	PRO	696	64.998	23.549	66.462	1.00	2.00	0
ATOM	4756	CB	PRO	696	64.997	22.163	65.803	1.00	5.25	0
ATOM	4757	CG	PRO	696	63.768	21.486	66.381	1.00	5.25	0
ATOM	4758	C	PRO	696	65.570	24.612	65.536	1.00	2.00	0
ATOM	4759	O	PRO	696	64.878	25.556	65.137	1.00	5.25	0
ATOM	4760	N	ASP	697	66.850	24.431	65.214	1.00	34.70	0
ATOM	4762	CA	ASP	697	67.598	25.311	64.321	1.00	35.10	0
ATOM	4763	CB	ASP	697	69.098	24.951	64.376	1.00	81.36	0
ATOM	4764	CG	ASP	697	69.630	24.774	65.825	1.00	81.80	0
ATOM	4765	OD1	ASP	697	69.612	23.613	66.347	1.00	0.89	0
ATOM	4766	OD2	ASP	697	70.075	25.792	66.436	1.00	0.05	0
ATOM	4767	C	ASP	697	67.037	25.099	62.894	1.00	36.63	0
ATOM	4768	O	ASP	697	67.014	26.022	62.069	1.00	0.75	0
ATOM	4769	N	GLN	698	66.576	23.877	62.620	1.00	8.48	0
ATOM	4771	CA	GLN	698	65.997	23.510	61.335	1.00	2.00	0
ATOM	4772	CB	GLN	698	67.089	23.346	60.285	1.00	43.65	0
ATOM	4773	CG	GLN	698	68.191	22.376	60.649	1.00	44.93	0
ATOM	4774	CD	GLN	698	69.158	22.169	59.501	1.00	43.25	0
ATOM	4775	OE1	GLN	698	68.781	22.242	58.327	1.00	45.90	0
ATOM	4776	NE2	GLN	698	70.411	21.911	59.830	1.00	44.14	0
ATOM	4779	C	GLN	698	65.211	22.216	61.482	1.00	2.32	0
ATOM	4780	O	GLN	698	65.396	21.486	62.452	1.00	42.62	0
ATOM	4781	N	GLY	699	64.324	21.939	60.530	1.00	2.00	0
ATOM	4783	CA	GLY	699	63.510	20.728	60.576	1.00	2.00	0
ATOM	4784	C	GLY	699	62.046	21.059	60.346	1.00	2.00	0
ATOM	4785	O	GLY	699	61.726	22.204	60.013	1.00	2.00	0
ATOM	4786	N	LEU	700	61.153	20.090	60.545	1.00	2.00	0
ATOM	4788	CA	LEU	700	59.700	20.297	60.352	1.00	2.00	0
ATOM	4789	CB	LEU	700	58.941	18.962	60.555	1.00	4.64	0
ATOM	4790	CG	LEU	700	57.436	18.836	60.273	1.00	8.84	0
ATOM	4791	CD1	LEU	700	57.219	18.881	58.793	1.00	8.28	0
ATOM	4792	CD2	LEU	700	56.879	17.536	60.803	1.00	5.23	0
ATOM	4793	C	LEU	700	59.086	21.400	61.247	1.00	2.00	0
ATOM	4794	O	LEU	700	58.365	22.261	60.763	1.00	8.77	0

ATOM	4795	N	LEU	701	59.394	21.381	62.540	1.00	12.05	0
ATOM	4797	CA	LEU	701	58.860	22.362	63.477	1.00	11.21	0
ATOM	4798	CB	LEU	701	59.278	22.039	64.908	1.00	2.00	0
ATOM	4799	CG	LEU	701	58.156	21.874	65.942	1.00	2.00	0
ATOM	4800	CD1	LEU	701	58.759	21.879	67.354	1.00	2.00	0
ATOM	4801	CD2	LEU	701	57.124	22.994	65.800	1.00	2.00	0
ATOM	4802	C	LEU	701	59.339	23.747	63.153	1.00	6.49	0
ATOM	4803	O	LEU	701	58.562	24.691	63.157	1.00	2.00	0
ATOM	4804	N	CYS	702	60.626	23.881	62.890	1.00	2.00	0
ATOM	4806	CA	CYS	702	61.158	25.191	62.572	1.00	2.00	0
ATOM	4807	CB	CYS	702	62.646	25.117	62.269	1.00	10.82	0
ATOM	4808	SG	CYS	702	63.290	26.639	61.543	1.00	10.82	0
ATOM	4809	C	CYS	702	60.442	25.786	61.365	1.00	2.00	0
ATOM	4810	O	CYS	702	60.022	26.954	61.384	1.00	10.82	0
ATOM	4811	N	ASP	703	60.292	24.980	60.316	1.00	2.00	0
ATOM	4813	CA	ASP	703	59.641	25.442	59.104	1.00	2.00	0
ATOM	4814	CB	ASP	703	59.790	24.391	58.010	1.00	9.22	0
ATOM	4815	CG	ASP	703	61.251	24.076	57.698	1.00	9.98	0
ATOM	4816	OD1	ASP	703	62.126	24.940	57.943	1.00	9.22	0
ATOM	4817	OD2	ASP	703	61.537	22.956	57.213	1.00	9.22	0
ATOM	4818	C	ASP	703	58.187	25.760	59.377	1.00	2.00	0
ATOM	4819	O	ASP	703	57.694	26.823	59.023	1.00	11.43	0
ATOM	4820	N	LEU	704	57.519	24.861	60.072	1.00	2.00	0
ATOM	4822	CA	LEU	704	56.113	25.051	60.391	1.00	2.00	0
ATOM	4823	CB	LEU	704	55.630	23.942	61.338	1.00	22.47	0
ATOM	4824	CG	LEU	704	55.412	22.533	60.780	1.00	21.16	0
ATOM	4825	CD1	LEU	704	55.366	21.528	61.911	1.00	24.29	0
ATOM	4826	CD2	LEU	704	54.132	22.489	59.973	1.00	22.40	0
ATOM	4827	C	LEU	704	55.809	26.417	61.006	1.00	2.00	0
ATOM	4828	O	LEU	704	54.736	26.979	60.773	1.00	15.38	0
ATOM	4829	N	LEU	705	56.757	26.967	61.763	1.00	39.58	0
ATOM	4831	CA	LEU	705	56.538	28.248	62.439	1.00	39.58	0
ATOM	4832	CB	LEU	705	56.884	28.108	63.913	1.00	2.00	0
ATOM	4833	CG	LEU	705	56.841	26.725	64.552	1.00	2.00	0
ATOM	4834	CD1	LEU	705	57.376	26.870	65.950	1.00	2.00	0
ATOM	4835	CD2	LEU	705	55.446	26.156	64.566	1.00	2.00	0
ATOM	4836	C	LEU	705	57.279	29.466	61.900	1.00	39.58	0
ATOM	4837	O	LEU	705	56.924	30.598	62.240	1.00	2.00	0
ATOM	4838	N	TRP	706	58.307	29.237	61.086	1.00	2.00	0
ATOM	4840	CA	TRP	706	59.117	30.319	60.523	1.00	2.00	0
ATOM	4841	CB	TRP	706	60.594	30.025	60.777	1.00	23.95	0
ATOM	4842	CG	TRP	706	61.025	30.261	62.165	1.00	23.95	0
ATOM	4843	CD2	TRP	706	61.380	31.520	62.742	1.00	23.95	0
ATOM	4844	CE2	TRP	706	61.735	31.278	64.083	1.00	23.95	0
ATOM	4845	CE3	TRP	706	61.434	32.832	62.254	1.00	23.95	0
ATOM	4846	CD1	TRP	706	61.173	29.329	63.150	1.00	23.95	0
ATOM	4847	NE1	TRP	706	61.599	29.932	64.307	1.00	23.95	0
ATOM	4849	CZ2	TRP	706	62.141	32.303	64.946	1.00	23.95	0
ATOM	4850	CZ3	TRP	706	61.835	33.850	63.108	1.00	23.95	0
ATOM	4851	CH2	TRP	706	62.184	33.580	64.439	1.00	23.95	0
ATOM	4852	C	TRP	706	58.947	30.619	59.028	1.00	2.00	0
ATOM	4853	O	TRP	706	59.186	31.751	58.598	1.00	23.95	0
ATOM	4854	N	SER	707	58.564	29.604	58.249	1.00	17.80	0
ATOM	4856	CA	SER	707	58.423	29.730	56.796	1.00	12.52	0
ATOM	4857	CB	SER	707	58.034	28.383	56.160	1.00	9.59	0
ATOM	4858	OG	SER	707	56.693	28.010	56.444	1.00	8.78	0
ATOM	4860	C	SER	707	57.459	30.806	56.328	1.00	18.86	0
ATOM	4861	O	SER	707	56.521	31.179	57.035	1.00	6.18	0
ATOM	4862	N	ASP	708	57.700	31.303	55.124	1.00	7.67	0
ATOM	4864	CA	ASP	708	56.860	32.328	54.547	1.00	7.67	0
ATOM	4865	CB	ASP	708	57.546	33.676	54.656	1.00	8.53	0
ATOM	4866	CG	ASP	708	57.720	34.104	56.079	1.00	10.12	0
ATOM	4867	OD1	ASP	708	58.844	34.049	56.597	1.00	10.18	0
ATOM	4868	OD2	ASP	708	56.717	34.483	56.689	1.00	10.95	0
ATOM	4869	C	ASP	708	56.609	31.998	53.104	1.00	7.67	0
ATOM	4870	O	ASP	708	57.461	31.432	52.444	1.00	11.43	0
ATOM	4871	N	PRO	709	55.425	32.328	52.596	1.00	2.00	0
ATOM	4872	CD	PRO	709	54.346	33.006	53.302	1.00	2.00	0

ATOM	4873	CA	PRO	709	55.029	32.078	51.214	1.00	2.00	0
ATOM	4874	CB	PRO	709	53.507	32.036	51.283	1.00	2.00	0
ATOM	4875	CG	PRO	709	53.169	32.316	52.728	1.00	2.00	0
ATOM	4876	C	PRO	709	55.475	33.269	50.406	1.00	2.00	0
ATOM	4877	O	PRO	709	55.071	34.393	50.712	1.00	2.00	0
ATOM	4878	N	ASP	710	56.306	33.046	49.393	1.00	2.57	0
ATOM	4880	CA	ASP	710	56.769	34.155	48.576	1.00	4.76	0
ATOM	4881	CB	ASP	710	58.297	34.215	48.537	1.00	18.70	0
ATOM	4882	CG	ASP	710	58.824	35.631	48.303	1.00	26.43	0
ATOM	4883	OD1	ASP	710	58.070	36.497	47.793	1.00	26.58	0
ATOM	4884	OD2	ASP	710	60.002	35.884	48.635	1.00	30.90	0
ATOM	4885	C	ASP	710	56.211	34.045	47.168	1.00	5.37	0
ATOM	4886	O	ASP	710	56.454	33.056	46.467	1.00	15.67	0
ATOM	4887	N	LYS	711	55.449	35.074	46.789	1.00	10.56	0
ATOM	4889	CA	LYS	711	54.802	35.217	45.480	1.00	16.19	0
ATOM	4890	CB	LYS	711	54.266	36.661	45.368	1.00	35.75	0
ATOM	4891	CG	LYS	711	53.743	37.109	44.007	1.00	43.76	0
ATOM	4892	CD	LYS	711	54.843	37.750	43.146	1.00	49.83	0
ATOM	4893	CE	LYS	711	55.459	38.976	43.819	1.00	54.70	0
ATOM	4894	NZ	LYS	711	56.632	39.514	43.064	1.00	58.93	0
ATOM	4898	C	LYS	711	55.753	34.877	44.331	1.00	16.03	0
ATOM	4899	O	LYS	711	55.459	34.001	43.518	1.00	37.96	0
ATOM	4900	N	ASP	712	56.894	35.560	44.282	1.00	2.00	0
ATOM	4902	CA	ASP	712	57.890	35.330	43.252	1.00	2.00	0
ATOM	4903	CB	ASP	712	58.655	36.629	42.927	1.00	75.12	0
ATOM	4904	CG	ASP	712	59.362	37.231	44.134	1.00	75.41	0
ATOM	4905	OD1	ASP	712	58.723	38.013	44.866	1.00	77.74	0
ATOM	4906	OD2	ASP	712	60.561	36.937	44.341	1.00	84.37	0
ATOM	4907	C	ASP	712	58.863	34.189	43.597	1.00	2.00	0
ATOM	4908	O	ASP	712	60.083	34.366	43.607	1.00	77.12	0
ATOM	4909	N	VAL	713	58.298	33.016	43.866	1.00	27.09	0
ATOM	4911	CA	VAL	713	59.057	31.811	44.188	1.00	17.74	0
ATOM	4912	CB	VAL	713	59.166	31.579	45.727	1.00	2.00	0
ATOM	4913	CG1	VAL	713	59.124	30.098	46.069	1.00	2.00	0
ATOM	4914	CG2	VAL	713	60.481	32.120	46.224	1.00	2.00	0
ATOM	4915	C	VAL	713	58.319	30.653	43.538	1.00	21.93	0
ATOM	4916	O	VAL	713	57.092	30.567	43.593	1.00	2.00	0
ATOM	4917	N	LEU	714	59.063	29.766	42.903	1.00	15.32	0
ATOM	4919	CA	LEU	714	58.434	28.642	42.249	1.00	10.30	0
ATOM	4920	CB	LEU	714	59.285	28.147	41.078	1.00	48.90	0
ATOM	4921	CG	LEU	714	58.662	27.005	40.272	1.00	42.23	0
ATOM	4922	CD1	LEU	714	57.229	27.357	39.909	1.00	43.72	0
ATOM	4923	CD2	LEU	714	59.478	26.753	39.025	1.00	42.86	0
ATOM	4924	C	LEU	714	58.224	27.530	43.235	1.00	13.23	0
ATOM	4925	O	LEU	714	57.096	27.099	43.445	1.00	44.72	0
ATOM	4926	N	GLY	715	59.322	27.075	43.834	1.00	76.36	0
ATOM	4928	CA	GLY	715	59.263	25.995	44.800	1.00	76.36	0
ATOM	4929	C	GLY	715	59.630	26.420	46.206	1.00	76.36	0
ATOM	4930	O	GLY	715	58.814	26.974	46.929	1.00	19.62	0
ATOM	4931	N	TRP	716	60.875	26.183	46.583	1.00	4.87	0
ATOM	4933	CA	TRP	716	61.365	26.503	47.918	1.00	4.87	0
ATOM	4934	CB	TRP	716	61.944	25.241	48.554	1.00	2.00	0
ATOM	4935	CG	TRP	716	60.884	24.317	48.932	1.00	2.00	0
ATOM	4936	CD2	TRP	716	59.936	24.529	49.962	1.00	2.00	0
ATOM	4937	CE2	TRP	716	59.050	23.439	49.943	1.00	2.00	0
ATOM	4938	CE3	TRP	716	59.750	25.541	50.909	1.00	2.00	0
ATOM	4939	CD1	TRP	716	60.562	23.134	48.343	1.00	2.00	0
ATOM	4940	NE1	TRP	716	59.454	22.597	48.940	1.00	2.00	0
ATOM	4942	CZ2	TRP	716	57.994	23.334	50.830	1.00	2.00	0
ATOM	4943	CZ3	TRP	716	58.715	25.438	51.783	1.00	2.00	0
ATOM	4944	CH2	TRP	716	57.843	24.343	51.743	1.00	2.00	0
ATOM	4945	C	TRP	716	62.406	27.594	47.954	1.00	4.87	0
ATOM	4946	O	TRP	716	63.596	27.315	47.871	1.00	2.00	0
ATOM	4947	N	GLY	717	61.968	28.837	48.067	1.00	2.00	0
ATOM	4949	CA	GLY	717	62.911	29.937	48.124	1.00	2.00	0
ATOM	4950	C	GLY	717	63.725	30.031	49.414	1.00	2.00	0
ATOM	4951	O	GLY	717	63.443	29.343	50.404	1.00	2.00	0
ATOM	4952	N	GLU	718	64.752	30.880	49.387	1.00	4.99	0

ATOM	4954	CA	GLU	718	65.606	31.113	50.538	1.00	8.49	0
ATOM	4955	CB	GLU	718	66.980	31.619	50.092	1.00	86.14	0
ATOM	4956	CG	GLU	718	68.026	31.716	51.211	1.00	89.35	0
ATOM	4957	CD	GLU	718	68.627	30.371	51.633	1.00	87.67	0
ATOM	4958	OE1	GLU	718	69.392	30.358	52.624	1.00	95.59	0
ATOM	4959	OE2	GLU	718	68.353	29.336	50.986	1.00	88.92	0
ATOM	4960	C	GLU	718	64.883	32.182	51.340	1.00	9.60	0
ATOM	4961	O	GLU	718	64.597	33.269	50.828	1.00	90.23	0
ATOM	4962	N	ASN	719	64.560	31.863	52.590	1.00	32.81	0
ATOM	4964	CA	ASN	719	63.848	32.804	53.444	1.00	33.93	0
ATOM	4965	CB	ASN	719	63.159	32.083	54.591	1.00	14.30	0
ATOM	4966	CG	ASN	719	62.159	32.965	55.296	1.00	14.30	0
ATOM	4967	OD1	ASN	719	62.533	33.912	55.983	1.00	14.30	0
ATOM	4968	ND2	ASN	719	60.879	32.676	55.110	1.00	14.30	0
ATOM	4971	C	ASN	719	64.781	33.855	54.007	1.00	33.45	0
ATOM	4972	O	ASN	719	65.825	33.529	54.566	1.00	14.30	0
ATOM	4973	N	ASP	720	64.388	35.117	53.878	1.00	42.61	0
ATOM	4975	CA	ASP	720	65.212	36.222	54.351	1.00	47.00	0
ATOM	4976	CB	ASP	720	64.744	37.535	53.706	1.00	77.30	0
ATOM	4977	CG	ASP	720	65.025	37.574	52.200	1.00	92.85	0
ATOM	4978	OD1	ASP	720	66.104	38.071	51.801	1.00	92.39	0
ATOM	4979	OD2	ASP	720	64.172	37.094	51.416	1.00	90.51	0
ATOM	4980	C	ASP	720	65.328	36.352	55.869	1.00	39.89	0
ATOM	4981	O	ASP	720	66.255	36.986	56.370	1.00	74.64	0
ATOM	4982	N	ARG	721	64.411	35.728	56.602	1.00	13.83	0
ATOM	4984	CA	ARG	721	64.446	35.759	58.060	1.00	12.18	0
ATOM	4985	CB	ARG	721	63.262	35.007	58.649	1.00	15.37	0
ATOM	4986	CG	ARG	721	61.946	35.693	58.572	1.00	7.28	0
ATOM	4987	CD	ARG	721	60.950	34.836	59.300	1.00	7.28	0
ATOM	4988	NE	ARG	721	59.593	35.306	59.103	1.00	8.88	0
ATOM	4990	CZ	ARG	721	59.051	36.315	59.766	1.00	9.83	0
ATOM	4991	NH1	ARG	721	59.751	36.965	60.690	1.00	8.95	0
ATOM	4994	NH2	ARG	721	57.809	36.682	59.485	1.00	8.62	0
ATOM	4997	C	ARG	721	65.710	35.093	58.592	1.00	8.44	0
ATOM	4998	O	ARG	721	65.982	35.142	59.798	1.00	10.25	0
ATOM	4999	N	GLY	722	66.449	34.437	57.697	1.00	4.85	0
ATOM	5001	CA	GLY	722	67.668	33.752	58.083	1.00	4.85	0
ATOM	5002	C	GLY	722	67.392	32.344	58.592	1.00	4.85	0
ATOM	5003	O	GLY	722	68.305	31.655	59.052	1.00	76.68	0
ATOM	5004	N	VAL	723	66.134	31.918	58.508	1.00	10.85	0
ATOM	5006	CA	VAL	723	65.717	30.591	58.958	1.00	10.85	0
ATOM	5007	CB	VAL	723	65.259	30.574	60.471	1.00	2.00	0
ATOM	5008	CG1	VAL	723	66.449	30.400	61.386	1.00	2.00	0
ATOM	5009	CG2	VAL	723	64.504	31.858	60.825	1.00	2.00	0
ATOM	5010	C	VAL	723	64.546	30.100	58.105	1.00	10.85	0
ATOM	5011	O	VAL	723	63.667	30.883	57.714	1.00	2.00	0
ATOM	5012	N	SER	724	64.541	28.802	57.824	1.00	42.15	0
ATOM	5014	CA	SER	724	63.479	28.193	57.040	1.00	42.15	0
ATOM	5015	CB	SER	724	62.127	28.609	57.623	1.00	2.00	0
ATOM	5016	OG	SER	724	61.077	27.808	57.106	1.00	2.00	0
ATOM	5018	C	SER	724	63.583	28.588	55.561	1.00	42.15	0
ATOM	5019	O	SER	724	64.680	28.820	55.049	1.00	2.00	0
ATOM	5020	N	PHE	725	62.454	28.643	54.863	1.00	2.00	0
ATOM	5022	CA	PHE	725	62.464	29.007	53.457	1.00	2.00	0
ATOM	5023	CB	PHE	725	62.461	27.779	52.541	1.00	2.00	0
ATOM	5024	CG	PHE	725	62.891	26.551	53.205	1.00	2.00	0
ATOM	5025	CD1	PHE	725	62.047	25.916	54.089	1.00	2.00	0
ATOM	5026	CD2	PHE	725	64.151	26.044	52.984	1.00	2.00	0
ATOM	5027	CE1	PHE	725	62.458	24.791	54.750	1.00	2.00	0
ATOM	5028	CE2	PHE	725	64.578	24.906	53.646	1.00	2.00	0
ATOM	5029	CZ	PHE	725	63.733	24.280	54.530	1.00	2.00	0
ATOM	5030	C	PHE	725	61.222	29.787	53.146	1.00	2.00	0
ATOM	5031	O	PHE	725	60.382	30.040	54.009	1.00	2.00	0
ATOM	5032	N	THR	726	61.132	30.162	51.886	1.00	34.54	0
ATOM	5034	CA	THR	726	60.009	30.877	51.357	1.00	30.82	0
ATOM	5035	CB	THR	726	60.468	32.154	50.661	1.00	2.00	0
ATOM	5036	OG1	THR	726	61.880	32.098	50.406	1.00	2.00	0
ATOM	5038	CG2	THR	726	60.222	33.327	51.561	1.00	2.00	0

ATOM	5039	C	THR	726	59.450	29.866	50.382	1.00	34.20	0
ATOM	5040	O	THR	726	60.201	29.208	49.684	1.00	2.00	0
ATOM	5041	N	PHE	727	58.144	29.685	50.375	1.00	2.00	0
ATOM	5043	CA	PHE	727	57.555	28.712	49.483	1.00	2.00	0
ATOM	5044	CB	PHE	727	56.852	27.612	50.275	1.00	9.97	0
ATOM	5045	CG	PHE	727	55.698	28.096	51.105	1.00	15.33	0
ATOM	5046	CD1	PHE	727	54.394	27.922	50.666	1.00	9.89	0
ATOM	5047	CD2	PHE	727	55.916	28.726	52.323	1.00	15.65	0
ATOM	5048	CE1	PHE	727	53.338	28.360	51.418	1.00	11.89	0
ATOM	5049	CE2	PHE	727	54.852	29.171	53.087	1.00	6.87	0
ATOM	5050	CZ	PHE	727	53.563	28.986	52.631	1.00	11.72	0
ATOM	5051	C	PHE	727	56.580	29.398	48.553	1.00	2.00	0
ATOM	5052	O	PHE	727	55.848	30.312	48.982	1.00	18.77	0
ATOM	5053	N	GLY	728	56.576	28.956	47.289	1.00	13.14	0
ATOM	5055	CA	GLY	728	55.709	29.542	46.277	1.00	12.12	0
ATOM	5056	C	GLY	728	54.348	28.894	46.174	1.00	13.69	0
ATOM	5057	O	GLY	728	54.062	27.913	46.862	1.00	2.00	0
ATOM	5058	N	ALA	729	53.513	29.436	45.292	1.00	33.39	0
ATOM	5060	CA	ALA	729	52.161	28.916	45.080	1.00	33.11	0
ATOM	5061	CB	ALA	729	51.375	29.862	44.200	1.00	16.31	0
ATOM	5062	C	ALA	729	52.139	27.507	44.485	1.00	31.34	0
ATOM	5063	O	ALA	729	51.143	26.796	44.600	1.00	16.31	0
ATOM	5064	N	GLU	730	53.221	27.105	43.831	1.00	22.53	0
ATOM	5066	CA	GLU	730	53.284	25.761	43.281	1.00	26.87	0
ATOM	5067	CB	GLU	730	54.622	25.551	42.570	1.00	59.75	0
ATOM	5068	CG	GLU	730	54.893	24.117	42.142	1.00	62.63	0
ATOM	5069	CD	GLU	730	56.138	23.984	41.283	1.00	68.00	0
ATOM	5070	OE1	GLU	730	57.213	23.624	41.822	1.00	74.97	0
ATOM	5071	OE2	GLU	730	56.034	24.238	40.063	1.00	67.31	0
ATOM	5072	C	GLU	730	53.140	24.781	44.446	1.00	24.85	0
ATOM	5073	O	GLU	730	52.285	23.899	44.425	1.00	58.27	0
ATOM	5074	N	VAL	731	53.958	24.989	45.477	1.00	24.13	0
ATOM	5076	CA	VAL	731	53.985	24.157	46.679	1.00	19.42	0
ATOM	5077	CB	VAL	731	55.079	24.628	47.645	1.00	19.11	0
ATOM	5078	CG1	VAL	731	55.159	23.699	48.824	1.00	19.11	0
ATOM	5079	CG2	VAL	731	56.412	24.691	46.942	1.00	19.11	0
ATOM	5080	C	VAL	731	52.659	24.165	47.423	1.00	16.89	0
ATOM	5081	O	VAL	731	52.210	23.128	47.900	1.00	19.11	0
ATOM	5082	N	VAL	732	52.035	25.332	47.525	1.00	15.54	0
ATOM	5084	CA	VAL	732	50.750	25.449	48.209	1.00	15.54	0
ATOM	5085	CB	VAL	732	50.254	26.898	48.240	1.00	20.17	0
ATOM	5086	CG1	VAL	732	48.907	26.985	48.962	1.00	20.17	0
ATOM	5087	CG2	VAL	732	51.272	27.764	48.902	1.00	20.17	0
ATOM	5088	C	VAL	732	49.653	24.609	47.554	1.00	15.54	0
ATOM	5089	O	VAL	732	49.011	23.791	48.222	1.00	20.17	0
ATOM	5090	N	ALA	733	49.437	24.822	46.253	1.00	16.29	0
ATOM	5092	CA	ALA	733	48.408	24.109	45.501	1.00	16.29	0
ATOM	5093	CB	ALA	733	48.260	24.717	44.131	1.00	17.33	0
ATOM	5094	C	ALA	733	48.703	22.618	45.390	1.00	16.29	0
ATOM	5095	O	ALA	733	47.776	21.795	45.349	1.00	17.78	0
ATOM	5096	N	LYS	734	49.996	22.287	45.348	1.00	2.00	0
ATOM	5098	CA	LYS	734	50.499	20.905	45.259	1.00	2.00	0
ATOM	5099	CB	LYS	734	52.012	20.936	45.015	1.00	23.03	0
ATOM	5100	CG	LYS	734	52.507	20.244	43.759	1.00	25.55	0
ATOM	5101	CD	LYS	734	52.696	21.212	42.594	1.00	35.13	0
ATOM	5102	CE	LYS	734	53.613	20.608	41.521	1.00	40.96	0
ATOM	5103	NZ	LYS	734	55.006	20.311	42.001	1.00	46.09	0
ATOM	5107	C	LYS	734	50.222	20.146	46.578	1.00	2.00	0
ATOM	5108	O	LYS	734	49.995	18.926	46.591	1.00	16.68	0
ATOM	5109	N	PHE	735	50.263	20.915	47.670	1.00	36.96	0
ATOM	5111	CA	PHE	735	50.036	20.478	49.047	1.00	33.73	0
ATOM	5112	CB	PHE	735	50.606	21.554	49.991	1.00	8.60	0
ATOM	5113	CG	PHE	735	50.320	21.323	51.465	1.00	8.60	0
ATOM	5114	CD1	PHE	735	50.955	20.298	52.169	1.00	8.60	0
ATOM	5115	CD2	PHE	735	49.412	22.135	52.142	1.00	8.60	0
ATOM	5116	CE1	PHE	735	50.690	20.086	53.512	1.00	8.60	0
ATOM	5117	CE2	PHE	735	49.143	21.929	53.483	1.00	8.60	0
ATOM	5118	CZ	PHE	735	49.784	20.900	54.168	1.00	8.60	0

ATOM	5119	C	PHE	735	48.546	20.256	49.334	1.00	34.15	0
ATOM	5120	O	PHE	735	48.151	19.181	49.801	1.00	8.60	0
ATOM	5121	N	LEU	736	47.731	21.281	49.075	1.00	2.00	0
ATOM	5123	CA	LEU	736	46.289	21.208	49.299	1.00	2.00	0
ATOM	5124	CB	LEU	736	45.599	22.451	48.770	1.00	2.00	0
ATOM	5125	CG	LEU	736	45.937	23.760	49.456	1.00	2.00	0
ATOM	5126	CD1	LEU	736	45.314	24.887	48.689	1.00	2.00	0
ATOM	5127	CD2	LEU	736	45.415	23.743	50.896	1.00	2.00	0
ATOM	5128	C	LEU	736	45.741	20.014	48.567	1.00	2.00	0
ATOM	5129	O	LEU	736	44.986	19.215	49.121	1.00	2.00	0
ATOM	5130	N	HIS	737	46.147	19.906	47.308	1.00	25.73	0
ATOM	5132	CA	HIS	737	45.747	18.818	46.427	1.00	25.73	0
ATOM	5133	CB	HIS	737	46.423	19.037	45.057	1.00	69.97	0
ATOM	5134	CG	HIS	737	46.638	17.784	44.263	1.00	68.65	0
ATOM	5135	CD2	HIS	737	47.779	17.169	43.868	1.00	71.13	0
ATOM	5136	ND1	HIS	737	45.601	17.012	43.783	1.00	76.45	0
ATOM	5138	CE1	HIS	737	46.093	15.974	43.129	1.00	76.42	0
ATOM	5139	NE2	HIS	737	47.412	16.046	43.166	1.00	74.54	0
ATOM	5141	C	HIS	737	46.088	17.440	47.037	1.00	25.73	0
ATOM	5142	O	HIS	737	45.223	16.570	47.166	1.00	61.28	0
ATOM	5143	N	LYS	738	47.347	17.266	47.422	1.00	11.82	0
ATOM	5145	CA	LYS	738	47.836	16.028	48.010	1.00	10.83	0
ATOM	5146	CB	LYS	738	49.343	16.163	48.256	1.00	10.15	0
ATOM	5147	CG	LYS	738	49.999	15.111	49.119	1.00	13.96	0
ATOM	5148	CD	LYS	738	51.516	15.253	49.005	1.00	16.98	0
ATOM	5149	CE	LYS	738	52.278	14.809	50.274	1.00	14.10	0
ATOM	5150	NZ	LYS	738	52.154	13.362	50.650	1.00	13.23	0
ATOM	5154	C	LYS	738	47.121	15.655	49.301	1.00	17.32	0
ATOM	5155	O	LYS	738	47.038	14.473	49.640	1.00	16.32	0
ATOM	5156	N	HIS	739	46.598	16.642	50.028	1.00	2.00	0
ATOM	5158	CA	HIS	739	45.935	16.319	51.284	1.00	2.00	0
ATOM	5159	CB	HIS	739	46.689	16.965	52.460	1.00	9.90	0
ATOM	5160	CG	HIS	739	48.099	16.482	52.597	1.00	8.91	0
ATOM	5161	CD2	HIS	739	48.603	15.318	53.077	1.00	3.85	0
ATOM	5162	ND1	HIS	739	49.182	17.212	52.148	1.00	7.65	0
ATOM	5164	CE1	HIS	739	50.291	16.517	52.340	1.00	6.50	0
ATOM	5165	NE2	HIS	739	49.966	15.364	52.901	1.00	3.85	0
ATOM	5167	C	HIS	739	44.442	16.598	51.378	1.00	2.00	0
ATOM	5168	O	HIS	739	43.913	16.722	52.477	1.00	18.58	0
ATOM	5169	N	ASP	740	43.763	16.678	50.236	1.00	2.00	0
ATOM	5171	CA	ASP	740	42.314	16.912	50.191	1.00	2.00	0
ATOM	5172	CB	ASP	740	41.567	15.695	50.758	1.00	37.08	0
ATOM	5173	CG	ASP	740	42.092	14.367	50.206	1.00	45.58	0
ATOM	5174	OD1	ASP	740	42.974	13.754	50.856	1.00	45.42	0
ATOM	5175	OD2	ASP	740	41.622	13.932	49.129	1.00	41.93	0
ATOM	5176	C	ASP	740	41.900	18.170	50.955	1.00	2.00	0
ATOM	5177	O	ASP	740	40.773	18.286	51.432	1.00	36.93	0
ATOM	5178	N	LEU	741	42.824	19.113	51.045	1.00	2.00	0
ATOM	5180	CA	LEU	741	42.610	20.357	51.764	1.00	2.00	0
ATOM	5181	CB	LEU	741	43.920	20.818	52.415	1.00	2.00	0
ATOM	5182	CG	LEU	741	44.572	19.861	53.388	1.00	2.00	0
ATOM	5183	CD1	LEU	741	45.906	20.394	53.859	1.00	2.00	0
ATOM	5184	CD2	LEU	741	43.620	19.673	54.519	1.00	2.00	0
ATOM	5185	C	LEU	741	42.122	21.433	50.818	1.00	2.00	0
ATOM	5186	O	LEU	741	42.261	21.301	49.611	1.00	2.00	0
ATOM	5187	N	ASP	742	41.588	22.510	51.385	1.00	2.00	0
ATOM	5189	CA	ASP	742	41.080	23.620	50.607	1.00	2.00	0
ATOM	5190	CB	ASP	742	39.605	23.858	50.909	1.00	21.53	0
ATOM	5191	CG	ASP	742	38.717	22.741	50.433	1.00	26.90	0
ATOM	5192	OD1	ASP	742	39.159	21.898	49.622	1.00	27.19	0
ATOM	5193	OD2	ASP	742	37.555	22.714	50.876	1.00	25.85	0
ATOM	5194	C	ASP	742	41.810	24.913	50.887	1.00	2.00	0
ATOM	5195	O	ASP	742	42.064	25.698	49.970	1.00	14.77	0
ATOM	5196	N	LEU	743	42.141	25.152	52.149	1.00	5.78	0
ATOM	5198	CA	LEU	743	42.785	26.407	52.509	1.00	5.78	0
ATOM	5199	CB	LEU	743	41.744	27.312	53.185	1.00	2.00	0
ATOM	5200	CG	LEU	743	41.689	28.847	53.088	1.00	2.00	0
ATOM	5201	CD1	LEU	743	40.947	29.364	54.297	1.00	2.00	0

ATOM	5202	CD2	LEU	743	43.051	29.469	53.053	1.00	2.00	0
ATOM	5203	C	LEU	743	43.919	26.152	53.483	1.00	5.78	0
ATOM	5204	O	LEU	743	43.973	25.091	54.088	1.00	2.00	0
ATOM	5205	N	ILE	744	44.837	27.104	53.599	1.00	2.00	0
ATOM	5207	CA	ILE	744	45.916	27.031	54.574	1.00	2.00	0
ATOM	5208	CB	ILE	744	47.338	27.043	53.968	1.00	2.00	0
ATOM	5209	CG2	ILE	744	48.360	27.214	55.089	1.00	2.00	0
ATOM	5210	CG1	ILE	744	47.637	25.754	53.204	1.00	2.00	0
ATOM	5211	CD1	ILE	744	49.117	25.602	52.856	1.00	2.00	0
ATOM	5212	C	ILE	744	45.770	28.330	55.356	1.00	2.00	0
ATOM	5213	O	ILE	744	45.830	29.423	54.788	1.00	2.00	0
ATOM	5214	N	CYS	745	45.557	28.226	56.655	1.00	71.57	0
ATOM	5216	CA	CYS	745	45.426	29.418	57.462	1.00	66.70	0
ATOM	5217	CB	CYS	745	44.204	29.301	58.363	1.00	17.55	0
ATOM	5218	SG	CYS	745	43.454	30.878	58.703	1.00	23.65	0
ATOM	5219	C	CYS	745	46.700	29.572	58.281	1.00	69.12	0
ATOM	5220	O	CYS	745	47.093	28.667	59.017	1.00	21.37	0
ATOM	5221	N	ARG	746	47.363	30.706	58.121	1.00	2.00	0
ATOM	5223	CA	ARG	746	48.594	30.982	58.837	1.00	2.00	0
ATOM	5224	CB	ARG	746	49.810	30.672	57.944	1.00	2.00	0
ATOM	5225	CG	ARG	746	49.860	31.394	56.609	1.00	2.00	0
ATOM	5226	CD	ARG	746	50.792	32.619	56.617	1.00	2.00	0
ATOM	5227	NE	ARG	746	52.220	32.293	56.560	1.00	2.00	0
ATOM	5229	CZ	ARG	746	53.212	33.184	56.626	1.00	2.00	0
ATOM	5230	NH1	ARG	746	52.956	34.479	56.738	1.00	2.00	0
ATOM	5233	NH2	ARG	746	54.468	32.778	56.603	1.00	2.00	0
ATOM	5236	C	ARG	746	48.597	32.439	59.271	1.00	2.00	0
ATOM	5237	O	ARG	746	47.739	33.220	58.847	1.00	2.00	0
ATOM	5238	N	ALA	747	49.524	32.802	60.146	1.00	2.00	0
ATOM	5240	CA	ALA	747	49.635	34.185	60.595	1.00	2.00	0
ATOM	5241	CB	ALA	747	49.410	34.264	62.106	1.00	2.00	0
ATOM	5242	C	ALA	747	51.073	34.588	60.193	1.00	2.00	0
ATOM	5243	O	ALA	747	51.378	34.658	58.999	1.00	2.00	0
ATOM	5244	N	HIS	748	51.943	34.854	61.168	1.00	2.00	0
ATOM	5246	CA	HIS	748	53.359	35.168	60.939	1.00	2.00	0
ATOM	5247	C	HIS	748	53.812	36.462	60.309	1.00	2.00	0
ATOM	5248	O	HIS	748	54.820	37.004	60.744	1.00	2.00	0
ATOM	5249	CB	HIS	748	54.032	34.028	60.187	1.00	2.00	0
ATOM	5250	CG	HIS	748	55.503	33.916	60.429	1.00	2.00	0
ATOM	5251	ND1	HIS	748	56.023	33.803	61.694	1.00	2.00	0
ATOM	5252	CE1	HIS	748	57.308	33.548	61.526	1.00	2.00	0
ATOM	5253	CD2	HIS	748	56.493	33.737	59.527	1.00	2.00	0
ATOM	5254	NE2	HIS	748	57.634	33.500	60.237	1.00	2.00	0
ATOM	5256	N	GLN	749	53.116	36.962	59.302	1.00	2.00	0
ATOM	5258	CA	GLN	749	53.556	38.197	58.677	1.00	2.00	0
ATOM	5259	CB	GLN	749	53.964	37.940	57.249	1.00	27.13	0
ATOM	5260	CG	GLN	749	55.257	37.222	57.143	1.00	28.03	0
ATOM	5261	CD	GLN	749	55.586	36.915	55.720	1.00	30.37	0
ATOM	5262	OE1	GLN	749	56.425	37.580	55.107	1.00	30.92	0
ATOM	5263	NE2	GLN	749	54.928	35.898	55.173	1.00	30.08	0
ATOM	5266	C	GLN	749	52.556	39.310	58.708	1.00	2.00	0
ATOM	5267	O	GLN	749	51.388	39.106	58.407	1.00	25.39	0
ATOM	5268	N	VAL	750	53.038	40.498	59.069	1.00	6.34	0
ATOM	5270	CA	VAL	750	52.193	41.682	59.157	1.00	6.34	0
ATOM	5271	CB	VAL	750	52.968	42.896	59.764	1.00	12.20	0
ATOM	5272	CG1	VAL	750	54.183	43.216	58.935	1.00	12.20	0
ATOM	5273	CG2	VAL	750	52.055	44.109	59.872	1.00	12.20	0
ATOM	5274	C	VAL	750	51.672	42.018	57.771	1.00	6.34	0
ATOM	5275	O	VAL	750	52.471	42.219	56.850	1.00	12.20	0
ATOM	5276	N	VAL	751	50.343	42.001	57.617	1.00	25.10	0
ATOM	5278	CA	VAL	751	49.685	42.327	56.348	1.00	25.10	0
ATOM	5279	CB	VAL	751	48.617	41.298	55.902	1.00	2.00	0
ATOM	5280	CG1	VAL	751	49.271	39.971	55.524	1.00	2.00	0
ATOM	5281	CG2	VAL	751	47.570	41.138	56.976	1.00	2.00	0
ATOM	5282	C	VAL	751	48.996	43.654	56.540	1.00	25.10	0
ATOM	5283	O	VAL	751	48.606	43.995	57.646	1.00	2.00	0
ATOM	5284	N	GLU	752	48.820	44.389	55.453	1.00	2.00	0
ATOM	5286	CA	GLU	752	48.219	45.709	55.526	1.00	2.00	0

ATOM	5287	CB	GLU	752	48.430	46.435	54.190	1.00	39.24	0
ATOM	5288	CG	GLU	752	49.867	46.349	53.628	1.00	75.32	0
ATOM	5289	CD	GLU	752	50.962	46.804	54.611	1.00	75.31	0
ATOM	5290	OE1	GLU	752	52.007	46.121	54.687	1.00	74.90	0
ATOM	5291	OE2	GLU	752	50.792	47.837	55.300	1.00	91.76	0
ATOM	5292	C	GLU	752	46.744	45.716	55.913	1.00	2.00	0
ATOM	5293	O	GLU	752	46.326	46.469	56.796	1.00	38.94	0
ATOM	5294	N	ASP	753	45.968	44.860	55.259	1.00	31.76	0
ATOM	5296	CA	ASP	753	44.527	44.776	55.491	1.00	34.73	0
ATOM	5297	CB	ASP	753	43.787	44.470	54.170	1.00	79.26	0
ATOM	5298	CG	ASP	753	44.539	43.487	53.251	1.00	85.10	0
ATOM	5299	OD1	ASP	753	44.040	43.240	52.130	1.00	88.01	0
ATOM	5300	OD2	ASP	753	45.613	42.960	53.619	1.00	92.40	0
ATOM	5301	C	ASP	753	44.028	43.853	56.606	1.00	31.43	0
ATOM	5302	O	ASP	753	42.824	43.759	56.835	1.00	64.64	0
ATOM	5303	N	GLY	754	44.940	43.188	57.309	1.00	8.60	0
ATOM	5305	CA	GLY	754	44.535	42.309	58.393	1.00	5.10	0
ATOM	5306	C	GLY	754	44.577	40.849	58.007	1.00	3.66	0
ATOM	5307	O	GLY	754	44.781	39.959	58.853	1.00	2.00	0
ATOM	5308	N	TYR	755	44.361	40.611	56.718	1.00	27.09	0
ATOM	5310	CA	TYR	755	44.388	39.282	56.129	1.00	27.09	0
ATOM	5311	CB	TYR	755	43.004	38.632	56.128	1.00	28.14	0
ATOM	5312	CG	TYR	755	41.976	39.338	55.279	1.00	25.47	0
ATOM	5313	CD1	TYR	755	41.236	40.393	55.797	1.00	23.65	0
ATOM	5314	CE1	TYR	755	40.276	41.049	55.034	1.00	28.13	0
ATOM	5315	CD2	TYR	755	41.736	38.949	53.964	1.00	30.24	0
ATOM	5316	CE2	TYR	755	40.774	39.601	53.187	1.00	27.11	0
ATOM	5317	CZ	TYR	755	40.046	40.653	53.732	1.00	32.27	0
ATOM	5318	OH	TYR	755	39.086	41.311	52.996	1.00	28.90	0
ATOM	5320	C	TYR	755	44.844	39.530	54.713	1.00	27.09	0
ATOM	5321	O	TYR	755	44.772	40.654	54.238	1.00	25.53	0
ATOM	5322	N	GLU	756	45.288	38.483	54.035	1.00	8.71	0
ATOM	5324	CA	GLU	756	45.787	38.617	52.676	1.00	8.71	0
ATOM	5325	CB	GLU	756	47.170	39.251	52.740	1.00	5.76	0
ATOM	5326	CG	GLU	756	47.832	39.557	51.436	1.00	16.72	0
ATOM	5327	CD	GLU	756	49.127	40.303	51.671	1.00	23.34	0
ATOM	5328	OE1	GLU	756	49.074	41.554	51.801	1.00	25.72	0
ATOM	5329	OE2	GLU	756	50.194	39.636	51.751	1.00	25.15	0
ATOM	5330	C	GLU	756	45.853	37.240	52.044	1.00	8.71	0
ATOM	5331	O	GLU	756	46.400	36.306	52.638	1.00	6.14	0
ATOM	5332	N	PHE	757	45.269	37.105	50.858	1.00	28.33	0
ATOM	5334	CA	PHE	757	45.270	35.822	50.174	1.00	28.33	0
ATOM	5335	CB	PHE	757	44.055	35.683	49.253	1.00	2.00	0
ATOM	5336	CG	PHE	757	42.748	35.612	49.982	1.00	2.00	0
ATOM	5337	CD1	PHE	757	41.961	36.747	50.137	1.00	2.00	0
ATOM	5338	CD2	PHE	757	42.306	34.407	50.535	1.00	2.00	0
ATOM	5339	CE1	PHE	757	40.751	36.695	50.833	1.00	2.00	0
ATOM	5340	CE2	PHE	757	41.092	34.337	51.238	1.00	2.00	0
ATOM	5341	CZ	PHE	757	40.315	35.489	51.385	1.00	2.00	0
ATOM	5342	C	PHE	757	46.547	35.639	49.387	1.00	28.33	0
ATOM	5343	O	PHE	757	47.220	36.602	49.033	1.00	2.00	0
ATOM	5344	N	PHE	758	46.893	34.387	49.150	1.00	2.00	0
ATOM	5346	CA	PHE	758	48.075	34.050	48.397	1.00	2.00	0
ATOM	5347	CB	PHE	758	49.241	33.789	49.317	1.00	10.52	0
ATOM	5348	CG	PHE	758	50.450	33.263	48.618	1.00	7.54	0
ATOM	5349	CD1	PHE	758	51.404	34.131	48.100	1.00	7.91	0
ATOM	5350	CD2	PHE	758	50.654	31.895	48.492	1.00	7.80	0
ATOM	5351	CE1	PHE	758	52.546	33.642	47.467	1.00	11.14	0
ATOM	5352	CE2	PHE	758	51.796	31.398	47.858	1.00	11.57	0
ATOM	5353	CZ	PHE	758	52.741	32.272	47.347	1.00	10.83	0
ATOM	5354	C	PHE	758	47.725	32.786	47.636	1.00	2.00	0
ATOM	5355	O	PHE	758	46.826	32.034	48.042	1.00	13.46	0
ATOM	5356	N	ALA	759	48.415	32.573	46.518	1.00	17.88	0
ATOM	5358	CA	ALA	759	48.196	31.407	45.673	1.00	17.63	0
ATOM	5359	CB	ALA	759	48.767	30.155	46.334	1.00	2.00	0
ATOM	5360	C	ALA	759	46.733	31.180	45.314	1.00	19.54	0
ATOM	5361	O	ALA	759	46.187	30.106	45.547	1.00	2.00	0
ATOM	5362	N	LYS	760	46.086	32.205	44.780	1.00	3.38	0

ATOM	5364	CA	LYS	760	44.699	32.076	44.341	1.00	3.38	0
ATOM	5365	CB	LYS	760	44.639	31.068	43.184	1.00	64.10	0
ATOM	5366	CG	LYS	760	45.654	31.316	42.062	1.00	64.10	0
ATOM	5367	CD	LYS	760	45.843	30.068	41.205	1.00	64.10	0
ATOM	5368	CE	LYS	760	44.506	29.540	40.699	1.00	64.10	0
ATOM	5369	NZ	LYS	760	44.621	28.293	39.896	1.00	64.10	0
ATOM	5373	C	LYS	760	43.715	31.659	45.432	1.00	3.38	0
ATOM	5374	O	LYS	760	42.953	30.702	45.256	1.00	64.10	0
ATOM	5375	N	ARG	761	43.751	32.376	46.557	1.00	16.83	0
ATOM	5377	CA	ARG	761	42.869	32.139	47.721	1.00	16.83	0
ATOM	5378	CB	ARG	761	41.399	32.154	47.274	1.00	38.86	0
ATOM	5379	CG	ARG	761	41.012	33.375	46.458	1.00	38.86	0
ATOM	5380	CD	ARG	761	40.550	34.493	47.334	1.00	38.86	0
ATOM	5381	NE	ARG	761	40.635	35.785	46.669	1.00	38.86	0
ATOM	5383	CZ	ARG	761	39.799	36.793	46.898	1.00	38.86	0
ATOM	5384	NH1	ARG	761	38.798	36.642	47.767	1.00	38.86	0
ATOM	5387	NH2	ARG	761	39.988	37.963	46.291	1.00	38.86	0
ATOM	5390	C	ARG	761	43.145	30.844	48.508	1.00	16.83	0
ATOM	5391	O	ARG	761	42.596	30.639	49.585	1.00	38.86	0
ATOM	5392	N	GLN	762	44.021	30.002	47.971	1.00	24.54	0
ATOM	5394	CA	GLN	762	44.359	28.718	48.559	1.00	24.54	0
ATOM	5395	CB	GLN	762	45.167	27.908	47.553	1.00	19.81	0
ATOM	5396	CG	GLN	762	44.502	27.794	46.173	1.00	19.81	0
ATOM	5397	CD	GLN	762	45.309	26.959	45.196	1.00	19.81	0
ATOM	5398	OE1	GLN	762	45.111	25.745	45.097	1.00	19.81	0
ATOM	5399	NE2	GLN	762	46.230	27.596	44.476	1.00	19.81	0
ATOM	5402	C	GLN	762	45.126	28.856	49.857	1.00	24.54	0
ATOM	5403	O	GLN	762	45.278	27.893	50.599	1.00	19.81	0
ATOM	5404	N	LEU	763	45.631	30.053	50.119	1.00	2.00	0
ATOM	5406	CA	LEU	763	46.354	30.326	51.353	1.00	2.00	0
ATOM	5407	CB	LEU	763	47.882	30.319	51.127	1.00	13.68	0
ATOM	5408	CG	LEU	763	48.847	30.427	52.335	1.00	13.68	0
ATOM	5409	CD1	LEU	763	50.117	29.641	52.066	1.00	13.68	0
ATOM	5410	CD2	LEU	763	49.200	31.871	52.633	1.00	13.68	0
ATOM	5411	C	LEU	763	45.893	31.705	51.809	1.00	2.00	0
ATOM	5412	O	LEU	763	45.654	32.595	50.981	1.00	13.68	0
ATOM	5413	N	VAL	764	45.741	31.869	53.118	1.00	13.21	0
ATOM	5415	CA	VAL	764	45.340	33.140	53.680	1.00	13.65	0
ATOM	5416	CB	VAL	764	43.825	33.165	53.953	1.00	2.00	0
ATOM	5417	CG1	VAL	764	43.452	32.097	54.933	1.00	2.00	0
ATOM	5418	CG2	VAL	764	43.404	34.521	54.434	1.00	2.00	0
ATOM	5419	C	VAL	764	46.159	33.363	54.955	1.00	18.12	0
ATOM	5420	O	VAL	764	46.396	32.437	55.737	1.00	2.00	0
ATOM	5421	N	THR	765	46.646	34.587	55.111	1.00	2.00	0
ATOM	5423	CA	THR	765	47.453	34.992	56.254	1.00	2.00	0
ATOM	5424	CB	THR	765	48.731	35.660	55.798	1.00	2.00	0
ATOM	5425	OG1	THR	765	49.474	34.740	54.991	1.00	2.00	0
ATOM	5427	CG2	THR	765	49.542	36.119	56.973	1.00	2.00	0
ATOM	5428	C	THR	765	46.675	36.024	57.030	1.00	2.00	0
ATOM	5429	O	THR	765	46.201	37.016	56.454	1.00	2.00	0
ATOM	5430	N	LEU	766	46.549	35.797	58.333	1.00	5.65	0
ATOM	5432	CA	LEU	766	45.832	36.717	59.205	1.00	5.65	0
ATOM	5433	CB	LEU	766	44.848	35.943	60.059	1.00	2.00	0
ATOM	5434	CG	LEU	766	43.964	34.922	59.372	1.00	2.00	0
ATOM	5435	CD1	LEU	766	43.703	33.794	60.327	1.00	2.00	0
ATOM	5436	CD2	LEU	766	42.672	35.581	58.943	1.00	2.00	0
ATOM	5437	C	LEU	766	46.826	37.382	60.142	1.00	5.65	0
ATOM	5438	O	LEU	766	47.864	36.790	60.478	1.00	2.00	0
ATOM	5439	N	PHE	767	46.520	38.605	60.554	1.00	2.00	0
ATOM	5441	CA	PHE	767	47.342	39.320	61.530	1.00	2.00	0
ATOM	5442	CB	PHE	767	48.259	40.328	60.864	1.00	2.00	0
ATOM	5443	CG	PHE	767	49.494	40.612	61.649	1.00	2.00	0
ATOM	5444	CD1	PHE	767	50.523	39.678	61.695	1.00	2.00	0
ATOM	5445	CD2	PHE	767	49.647	41.811	62.317	1.00	2.00	0
ATOM	5446	CE1	PHE	767	51.689	39.935	62.389	1.00	2.00	0
ATOM	5447	CE2	PHE	767	50.813	42.078	63.018	1.00	2.00	0
ATOM	5448	CZ	PHE	767	51.838	41.134	63.050	1.00	2.00	0
ATOM	5449	C	PHE	767	46.325	40.033	62.418	1.00	2.00	0

ATOM	5450	O	PHE	767	45.957	41.184	62.171	1.00	2.00	0
ATOM	5451	N	SER	768	45.850	39.317	63.432	1.00	2.00	0
ATOM	5453	CA	SER	768	44.833	39.819	64.334	1.00	2.00	0
ATOM	5454	CB	SER	768	44.247	38.645	65.091	1.00	2.00	0
ATOM	5455	OG	SER	768	43.903	37.635	64.175	1.00	2.00	0
ATOM	5457	C	SER	768	45.261	40.872	65.336	1.00	2.00	0
ATOM	5458	O	SER	768	46.297	40.731	65.973	1.00	2.00	0
ATOM	5459	N	ALA	769	44.435	41.911	65.474	1.00	30.20	0
ATOM	5461	CA	ALA	769	44.619	43.009	66.428	1.00	27.69	0
ATOM	5462	CB	ALA	769	45.142	42.454	67.786	1.00	4.86	0
ATOM	5463	C	ALA	769	45.410	44.253	66.018	1.00	31.35	0
ATOM	5464	O	ALA	769	44.855	45.347	65.940	1.00	11.84	0
ATOM	5465	N	PRO	770	46.717	44.109	65.786	1.00	14.07	0
ATOM	5466	CD	PRO	770	47.556	42.904	65.939	1.00	2.00	0
ATOM	5467	CA	PRO	770	47.578	45.209	65.398	1.00	14.07	0
ATOM	5468	CB	PRO	770	48.615	44.494	64.540	1.00	2.00	0
ATOM	5469	CG	PRO	770	48.913	43.329	65.392	1.00	2.00	0
ATOM	5470	C	PRO	770	47.227	46.584	64.825	1.00	14.07	0
ATOM	5471	O	PRO	770	46.081	47.016	64.640	1.00	2.00	0
ATOM	5472	N	ASN	771	48.363	47.259	64.718	1.00	2.00	0
ATOM	5474	CA	ASN	771	48.703	48.578	64.220	1.00	2.00	0
ATOM	5475	CB	ASN	771	48.014	49.664	65.022	1.00	40.66	0
ATOM	5476	CG	ASN	771	48.270	51.032	64.457	1.00	47.17	0
ATOM	5477	OD1	ASN	771	49.382	51.557	64.550	1.00	40.36	0
ATOM	5478	ND2	ASN	771	47.249	51.617	63.841	1.00	43.79	0
ATOM	5481	C	ASN	771	50.174	48.414	64.666	1.00	2.00	0
ATOM	5482	O	ASN	771	50.811	49.318	65.208	1.00	50.90	0
ATOM	5483	N	TYR	772	50.657	47.191	64.417	1.00	6.11	0
ATOM	5485	CA	TYR	772	51.955	46.645	64.768	1.00	6.11	0
ATOM	5486	CB	TYR	772	52.366	45.641	63.705	1.00	8.06	0
ATOM	5487	CG	TYR	772	53.253	44.546	64.228	1.00	8.06	0
ATOM	5488	CD1	TYR	772	52.992	43.949	65.453	1.00	8.06	0
ATOM	5489	CE1	TYR	772	53.781	42.910	65.929	1.00	8.06	0
ATOM	5490	CD2	TYR	772	54.335	44.084	63.487	1.00	8.06	0
ATOM	5491	CE2	TYR	772	55.135	43.048	63.945	1.00	8.06	0
ATOM	5492	CZ	TYR	772	54.854	42.459	65.170	1.00	8.06	0
ATOM	5493	OH	TYR	772	55.634	41.403	65.632	1.00	8.06	0
ATOM	5495	C	TYR	772	53.130	47.557	65.074	1.00	6.11	0
ATOM	5496	O	TYR	772	53.499	48.428	64.271	1.00	19.22	0
ATOM	5497	N	CYS	773	53.724	47.335	66.244	1.00	15.64	0
ATOM	5499	CA	CYS	773	54.868	48.107	66.681	1.00	13.08	0
ATOM	5500	CB	CYS	773	56.059	47.798	65.777	1.00	21.47	0
ATOM	5501	SG	CYS	773	56.646	46.112	65.891	1.00	23.28	0
ATOM	5502	C	CYS	773	54.624	49.617	66.685	1.00	16.93	0
ATOM	5503	O	CYS	773	55.573	50.398	66.832	1.00	20.82	0
ATOM	5504	N	GLY	774	53.362	50.031	66.545	1.00	2.00	0
ATOM	5506	CA	GLY	774	53.059	51.452	66.482	1.00	2.00	0
ATOM	5507	C	GLY	774	53.821	52.023	65.288	1.00	2.00	0
ATOM	5508	O	GLY	774	54.051	53.233	65.188	1.00	60.37	0
ATOM	5509	N	GLU	775	54.219	51.130	64.383	1.00	22.26	0
ATOM	5511	CA	GLU	775	54.973	51.500	63.211	1.00	18.01	0
ATOM	5512	CB	GLU	775	56.253	50.683	63.133	1.00	40.50	0
ATOM	5513	CG	GLU	775	57.103	50.811	64.357	1.00	44.10	0
ATOM	5514	CD	GLU	775	58.496	50.246	64.190	1.00	42.58	0
ATOM	5515	OE1	GLU	775	59.404	50.734	64.894	1.00	46.10	0
ATOM	5516	OE2	GLU	775	58.687	49.324	63.367	1.00	44.55	0
ATOM	5517	C	GLU	775	54.181	51.268	61.945	1.00	16.06	0
ATOM	5518	O	GLU	775	54.133	52.118	61.051	1.00	34.47	0
ATOM	5519	N	PHE	776	53.530	50.125	61.874	1.00	21.64	0
ATOM	5521	CA	PHE	776	52.809	49.796	60.667	1.00	19.45	0
ATOM	5522	CB	PHE	776	52.828	48.279	60.517	1.00	7.64	0
ATOM	5523	CG	PHE	776	54.213	47.739	60.363	1.00	6.06	0
ATOM	5524	CD1	PHE	776	55.056	47.656	61.452	1.00	6.54	0
ATOM	5525	CD2	PHE	776	54.692	47.363	59.122	1.00	10.09	0
ATOM	5526	CE1	PHE	776	56.370	47.206	61.313	1.00	6.06	0
ATOM	5527	CE2	PHE	776	56.005	46.910	58.969	1.00	9.96	0
ATOM	5528	CZ	PHE	776	56.845	46.833	60.071	1.00	6.06	0
ATOM	5529	C	PHE	776	51.424	50.402	60.480	1.00	21.71	0

ATOM	5530	O	PHE	776	50.979	50.601	59.346	1.00	9.78	0
ATOM	5531	N	ASP	777	50.757	50.720	61.584	1.00	47.34	0
ATOM	5533	CA	ASP	777	49.427	51.322	61.532	1.00	47.73	0
ATOM	5534	CB	ASP	777	49.526	52.790	61.071	1.00	36.82	0
ATOM	5535	CG	ASP	777	50.299	53.677	62.059	1.00	86.03	0
ATOM	5536	OD1	ASP	777	51.519	53.464	62.246	1.00	85.84	0
ATOM	5537	OD2	ASP	777	49.685	54.595	62.644	1.00	85.92	0
ATOM	5538	C	ASP	777	48.456	50.547	60.632	1.00	47.70	0
ATOM	5539	O	ASP	777	47.458	51.095	60.164	1.00	37.69	0
ATOM	5540	N	ASN	778	48.756	49.268	60.419	1.00	12.97	0
ATOM	5542	CA	ASN	778	47.948	48.373	59.584	1.00	3.97	0
ATOM	5543	CB	ASN	778	48.760	47.123	59.221	1.00	17.34	0
ATOM	5544	CG	ASN	778	49.081	46.258	60.435	1.00	11.19	0
ATOM	5545	OD1	ASN	778	49.928	46.613	61.275	1.00	10.18	0
ATOM	5546	ND2	ASN	778	48.404	45.120	60.538	1.00	7.69	0
ATOM	5549	C	ASN	778	46.672	47.945	60.296	1.00	4.32	0
ATOM	5550	O	ASN	778	46.497	48.227	61.481	1.00	21.92	0
ATOM	5551	N	ALA	779	45.783	47.267	59.578	1.00	6.26	0
ATOM	5553	CA	ALA	779	44.537	46.799	60.168	1.00	6.26	0
ATOM	5554	CB	ALA	779	43.404	46.923	59.174	1.00	78.54	0
ATOM	5555	C	ALA	779	44.727	45.344	60.580	1.00	6.26	0
ATOM	5556	O	ALA	779	45.537	44.626	59.988	1.00	86.19	0
ATOM	5557	N	GLY	780	43.998	44.925	61.606	1.00	2.00	0
ATOM	5559	CA	GLY	780	44.091	43.560	62.077	1.00	2.00	0
ATOM	5560	C	GLY	780	42.800	42.848	61.747	1.00	2.00	0
ATOM	5561	O	GLY	780	41.725	43.433	61.869	1.00	21.77	0
ATOM	5562	N	ALA	781	42.880	41.587	61.345	1.00	2.00	0
ATOM	5564	CA	ALA	781	41.670	40.870	60.984	1.00	2.00	0
ATOM	5565	CB	ALA	781	41.671	40.567	59.492	1.00	14.58	0
ATOM	5566	C	ALA	781	41.474	39.587	61.763	1.00	2.00	0
ATOM	5567	O	ALA	781	42.396	39.076	62.398	1.00	14.58	0
ATOM	5568	N	MET	782	40.263	39.061	61.660	1.00	2.00	0
ATOM	5570	CA	MET	782	39.857	37.833	62.319	1.00	2.00	0
ATOM	5571	CB	MET	782	39.037	38.204	63.554	1.00	2.00	0
ATOM	5572	CG	MET	782	38.736	37.067	64.502	1.00	2.00	0
ATOM	5573	SD	MET	782	37.743	37.608	65.912	1.00	2.00	0
ATOM	5574	CE	MET	782	37.595	39.370	65.621	1.00	2.00	0
ATOM	5575	C	MET	782	39.010	37.029	61.306	1.00	2.00	0
ATOM	5576	O	MET	782	38.090	37.570	60.688	1.00	2.00	0
ATOM	5577	N	MET	783	39.325	35.752	61.116	1.00	2.00	0
ATOM	5579	CA	MET	783	38.570	34.955	60.165	1.00	2.00	0
ATOM	5580	CB	MET	783	39.482	34.182	59.209	1.00	16.43	0
ATOM	5581	CG	MET	783	38.688	33.363	58.165	1.00	19.34	0
ATOM	5582	SD	MET	783	39.689	32.337	57.060	1.00	18.69	0
ATOM	5583	CE	MET	783	39.780	30.793	57.975	1.00	21.53	0
ATOM	5584	C	MET	783	37.608	33.976	60.794	1.00	2.00	0
ATOM	5585	O	MET	783	38.004	33.010	61.447	1.00	10.33	0
ATOM	5586	N	SER	784	36.335	34.221	60.542	1.00	2.00	0
ATOM	5588	CA	SER	784	35.276	33.374	61.034	1.00	2.00	0
ATOM	5589	CB	SER	784	34.033	34.220	61.308	1.00	16.25	0
ATOM	5590	OG	SER	784	34.385	35.392	62.020	1.00	16.25	0
ATOM	5592	C	SER	784	34.953	32.301	59.990	1.00	2.00	0
ATOM	5593	O	SER	784	34.672	32.611	58.839	1.00	19.28	0
ATOM	5594	N	VAL	785	35.033	31.045	60.401	1.00	10.88	0
ATOM	5596	CA	VAL	785	34.706	29.907	59.557	1.00	16.53	0
ATOM	5597	CB	VAL	785	35.649	28.739	59.792	1.00	11.43	0
ATOM	5598	CG1	VAL	785	35.183	27.538	58.975	1.00	11.43	0
ATOM	5599	CG2	VAL	785	37.082	29.153	59.477	1.00	11.43	0
ATOM	5600	C	VAL	785	33.357	29.465	60.083	1.00	12.38	0
ATOM	5601	O	VAL	785	33.254	28.998	61.225	1.00	11.43	0
ATOM	5602	N	ASP	786	32.307	29.613	59.291	1.00	2.00	0
ATOM	5604	CA	ASP	786	31.024	29.200	59.807	1.00	2.00	0
ATOM	5605	CB	ASP	786	29.874	30.008	59.171	1.00	24.90	0
ATOM	5606	CG	ASP	786	29.403	29.458	57.842	1.00	30.71	0
ATOM	5607	OD1	ASP	786	28.245	29.765	57.474	1.00	33.80	0
ATOM	5608	OD2	ASP	786	30.165	28.737	57.163	1.00	32.56	0
ATOM	5609	C	ASP	786	30.860	27.699	59.656	1.00	2.00	0
ATOM	5610	O	ASP	786	31.677	27.025	59.031	1.00	23.30	0

ATOM	5611	N	GLU	787	29.803	27.195	60.268	1.00	7.48	0
ATOM	5613	CA	GLU	787	29.447	25.782	60.270	1.00	13.41	0
ATOM	5614	CB	GLU	787	27.983	25.636	60.696	1.00	2.00	0
ATOM	5615	CG	GLU	787	27.174	26.963	60.747	1.00	2.00	0
ATOM	5616	CD	GLU	787	27.384	27.758	62.053	1.00	2.00	0
ATOM	5617	OE1	GLU	787	26.858	27.319	63.117	1.00	2.00	0
ATOM	5618	OE2	GLU	787	28.070	28.817	62.024	1.00	2.00	0
ATOM	5619	C	GLU	787	29.665	25.015	58.965	1.00	11.86	0
ATOM	5620	O	GLU	787	30.002	23.830	58.994	1.00	2.00	0
ATOM	5621	N	THR	788	29.492	25.698	57.836	1.00	56.74	0
ATOM	5623	CA	THR	788	29.616	25.092	56.513	1.00	52.70	0
ATOM	5624	CB	THR	788	28.369	25.402	55.700	1.00	6.46	0
ATOM	5625	OG1	THR	788	28.317	26.819	55.467	1.00	4.65	0
ATOM	5627	CG2	THR	788	27.101	24.968	56.457	1.00	10.48	0
ATOM	5628	C	THR	788	30.835	25.536	55.683	1.00	51.86	0
ATOM	5629	O	THR	788	30.751	25.628	54.449	1.00	12.46	0
ATOM	5630	N	LEU	789	31.946	25.823	56.364	1.00	10.40	0
ATOM	5632	CA	LEU	789	33.194	26.245	55.734	1.00	6.34	0
ATOM	5633	CB	LEU	789	33.670	25.165	54.775	1.00	8.80	0
ATOM	5634	CG	LEU	789	34.458	24.017	55.405	1.00	15.93	0
ATOM	5635	CD1	LEU	789	35.879	24.487	55.677	1.00	11.55	0
ATOM	5636	CD2	LEU	789	33.785	23.525	56.682	1.00	14.98	0
ATOM	5637	C	LEU	789	33.173	27.619	55.042	1.00	4.53	0
ATOM	5638	O	LEU	789	34.065	27.948	54.248	1.00	8.97	0
ATOM	5639	N	MET	790	32.165	28.430	55.336	1.00	2.00	0
ATOM	5641	CA	MET	790	32.126	29.748	54.743	1.00	2.00	0
ATOM	5642	CB	MET	790	30.698	30.267	54.636	1.00	19.79	0
ATOM	5643	CG	MET	790	30.588	31.572	53.882	1.00	19.37	0
ATOM	5644	SD	MET	790	28.979	31.708	53.134	1.00	18.51	0
ATOM	5645	CE	MET	790	28.359	33.110	53.992	1.00	23.23	0
ATOM	5646	C	MET	790	32.945	30.667	55.627	1.00	2.00	0
ATOM	5647	O	MET	790	32.615	30.857	56.799	1.00	23.79	0
ATOM	5648	N	CYS	791	34.014	31.228	55.067	1.00	2.00	0
ATOM	5650	CA	CYS	791	34.882	32.133	55.803	1.00	2.00	0
ATOM	5651	CB	CYS	791	36.325	31.793	55.516	1.00	14.83	0
ATOM	5652	SG	CYS	791	36.570	30.052	55.766	1.00	15.43	0
ATOM	5653	C	CYS	791	34.616	33.591	55.502	1.00	2.00	0
ATOM	5654	O	CYS	791	34.314	33.961	54.371	1.00	21.84	0
ATOM	5655	N	SER	792	34.697	34.412	56.540	1.00	2.00	0
ATOM	5657	CA	SER	792	34.480	35.849	56.430	1.00	2.00	0
ATOM	5658	CB	SER	792	33.073	36.221	56.903	1.00	2.93	0
ATOM	5659	OG	SER	792	32.887	35.867	58.256	1.00	3.41	0
ATOM	5661	C	SER	792	35.539	36.518	57.303	1.00	2.00	0
ATOM	5662	O	SER	792	36.290	35.826	57.994	1.00	2.56	0
ATOM	5663	N	PHE	793	35.609	37.842	57.270	1.00	2.00	0
ATOM	5665	CA	PHE	793	36.617	38.558	58.039	1.00	2.00	0
ATOM	5666	CB	PHE	793	37.765	39.025	57.129	1.00	38.05	0
ATOM	5667	CG	PHE	793	38.531	37.913	56.469	1.00	24.74	0
ATOM	5668	CD1	PHE	793	38.055	37.314	55.306	1.00	28.08	0
ATOM	5669	CD2	PHE	793	39.741	37.474	57.002	1.00	26.11	0
ATOM	5670	CE1	PHE	793	38.774	36.295	54.680	1.00	27.84	0
ATOM	5671	CE2	PHE	793	40.466	36.460	56.389	1.00	27.16	0
ATOM	5672	CZ	PHE	793	39.983	35.868	55.225	1.00	29.41	0
ATOM	5673	C	PHE	793	36.101	39.782	58.784	1.00	2.00	0
ATOM	5674	O	PHE	793	35.362	40.599	58.233	1.00	23.22	0
ATOM	5675	N	GLN	794	36.480	39.893	60.051	1.00	67.38	0
ATOM	5677	CA	GLN	794	36.128	41.064	60.837	1.00	63.52	0
ATOM	5678	CB	GLN	794	35.608	40.713	62.238	1.00	31.74	0
ATOM	5679	CG	GLN	794	34.294	39.954	62.289	1.00	36.03	0
ATOM	5680	CD	GLN	794	34.506	38.455	62.252	1.00	39.99	0
ATOM	5681	OE1	GLN	794	34.622	37.858	61.179	1.00	39.14	0
ATOM	5682	NE2	GLN	794	34.575	37.838	63.425	1.00	44.72	0
ATOM	5685	C	GLN	794	37.471	41.760	60.958	1.00	65.96	0
ATOM	5686	O	GLN	794	38.486	41.132	61.272	1.00	37.24	0
ATOM	5687	N	ILE	795	37.498	43.045	60.658	1.00	53.07	0
ATOM	5689	CA	ILE	795	38.732	43.790	60.748	1.00	54.05	0
ATOM	5690	CB	ILE	795	39.084	44.483	59.392	1.00	26.19	0
ATOM	5691	CG2	ILE	795	40.115	45.589	59.608	1.00	28.70	0

ATOM	5692	CG1	ILE	795	39.643	43.467	58.390	1.00	30.47	0
ATOM	5693	CD1	ILE	795	38.659	42.449	57.906	1.00	28.83	0
ATOM	5694	C	ILE	795	38.543	44.847	61.817	1.00	53.94	0
ATOM	5695	O	ILE	795	37.476	45.452	61.903	1.00	27.08	0
ATOM	5696	N	LEU	796	39.544	45.008	62.674	1.00	30.60	0
ATOM	5698	CA	LEU	796	39.521	46.054	63.686	1.00	34.91	0
ATOM	5699	CB	LEU	796	39.839	45.528	65.089	1.00	41.88	0
ATOM	5700	CG	LEU	796	40.368	44.121	65.308	1.00	41.67	0
ATOM	5701	CD1	LEU	796	40.976	44.038	66.702	1.00	39.26	0
ATOM	5702	CD2	LEU	796	39.242	43.114	65.119	1.00	42.51	0
ATOM	5703	C	LEU	796	40.637	46.977	63.206	1.00	33.78	0
ATOM	5704	O	LEU	796	41.649	46.510	62.667	1.00	34.59	0
ATOM	5705	N	LYS	797	40.454	48.280	63.356	1.00	37.84	0
ATOM	5707	CA	LYS	797	41.475	49.207	62.902	1.00	40.12	0
ATOM	5708	CB	LYS	797	40.805	50.354	62.154	1.00	0.26	0
ATOM	5709	CG	LYS	797	39.959	49.929	60.932	1.00	0.34	0
ATOM	5710	CD	LYS	797	39.456	51.183	60.151	1.00	0.65	0
ATOM	5711	CE	LYS	797	39.134	50.875	58.662	1.00	0.12	0
ATOM	5712	NZ	LYS	797	38.852	52.117	57.851	1.00	0.70	0
ATOM	5716	C	LYS	797	42.356	49.727	64.053	1.00	50.42	0
ATOM	5717	O	LYS	797	42.961	50.809	63.985	1.00	0.89	0
ATOM	5718	N	ALA	400	-8.399	33.628	131.469	1.00	75.56	0
ATOM	5720	CA	ALA	400	-6.981	33.565	131.818	1.00	75.56	0
ATOM	5721	CB	ALA	400	-6.134	33.160	130.576	1.00	21.27	0
ATOM	5722	C	ALA	400	-6.530	34.922	132.352	1.00	75.56	0
ATOM	5723	O	ALA	400	-7.350	35.762	132.744	1.00	21.27	0
ATOM	5724	N	ARG	401	-5.218	35.116	132.374	1.00	2.00	0
ATOM	5726	CA	ARG	401	-4.619	36.351	132.833	1.00	2.00	0
ATOM	5727	CB	ARG	401	-4.586	36.395	134.359	1.00	2.00	0
ATOM	5728	CG	ARG	401	-5.638	37.360	134.956	1.00	2.00	0
ATOM	5729	CD	ARG	401	-5.639	37.340	136.471	1.00	2.00	0
ATOM	5730	NE	ARG	401	-6.285	38.512	137.058	1.00	2.00	0
ATOM	5732	CZ	ARG	401	-5.730	39.260	138.022	1.00	2.00	0
ATOM	5733	NH1	ARG	401	-6.338	40.369	138.457	1.00	2.00	0
ATOM	5736	NH2	ARG	401	-4.527	38.949	138.511	1.00	2.00	0
ATOM	5739	C	ARG	401	-3.216	36.446	132.267	1.00	2.00	0
ATOM	5740	O	ARG	401	-2.505	35.443	132.150	1.00	2.00	0
ATOM	5741	N	VAL	402	-2.822	37.655	131.898	1.00	2.00	0
ATOM	5743	CA	VAL	402	-1.516	37.882	131.311	1.00	2.00	0
ATOM	5744	CB	VAL	402	-1.331	39.379	131.042	1.00	2.00	0
ATOM	5745	CG1	VAL	402	-0.063	39.632	130.283	1.00	2.00	0
ATOM	5746	CG2	VAL	402	-2.503	39.889	130.282	1.00	2.00	0
ATOM	5747	C	VAL	402	-0.398	37.376	132.223	1.00	2.00	0
ATOM	5748	O	VAL	402	-0.548	37.369	133.444	1.00	2.00	0
ATOM	5749	N	SER	403	0.701	36.920	131.625	1.00	19.26	0
ATOM	5751	CA	SER	403	1.882	36.461	132.361	1.00	23.92	0
ATOM	5752	CB	SER	403	1.894	34.942	132.528	1.00	22.54	0
ATOM	5753	OG	SER	403	1.503	34.298	131.333	1.00	14.30	0
ATOM	5755	C	SER	403	3.070	36.913	131.514	1.00	21.44	0
ATOM	5756	O	SER	403	2.890	37.720	130.595	1.00	23.72	0
ATOM	5757	N	PHE	404	4.271	36.415	131.793	1.00	13.47	0
ATOM	5759	CA	PHE	404	5.439	36.827	131.013	1.00	13.06	0
ATOM	5760	CB	PHE	404	6.101	38.060	131.647	1.00	2.00	0
ATOM	5761	CG	PHE	404	5.228	39.270	131.627	1.00	2.00	0
ATOM	5762	CD1	PHE	404	4.421	39.574	132.711	1.00	2.00	0
ATOM	5763	CD2	PHE	404	5.171	40.080	130.505	1.00	2.00	0
ATOM	5764	CE1	PHE	404	3.560	40.668	132.677	1.00	2.00	0
ATOM	5765	CE2	PHE	404	4.313	41.178	130.463	1.00	2.00	0
ATOM	5766	CZ	PHE	404	3.507	41.472	131.549	1.00	2.00	0
ATOM	5767	C	PHE	404	6.476	35.735	130.791	1.00	16.54	0
ATOM	5768	O	PHE	404	6.472	34.720	131.489	1.00	2.00	0
ATOM	5769	N	ALA	405	7.341	35.960	129.802	1.00	2.00	0
ATOM	5771	CA	ALA	405	8.420	35.054	129.414	1.00	2.00	0
ATOM	5772	CB	ALA	405	9.762	35.742	129.619	1.00	85.03	0
ATOM	5773	C	ALA	405	8.434	33.682	130.078	1.00	2.00	0
ATOM	5774	O	ALA	405	8.380	32.654	129.401	1.00	85.03	0
ATOM	5775	N	GLY	899	32.968	17.226	49.661	1.00	95.94	0
ATOM	5777	CA	GLY	899	31.781	16.989	50.464	1.00	95.94	0

ATOM	5778	C	GLY	899	31.215	18.274	51.038	1.00	95.94	0
ATOM	5779	O	GLY	899	30.022	18.368	51.338	1.00	32.75	0
ATOM	5780	N	ARG	900	32.090	19.260	51.193	1.00	42.23	0
ATOM	5782	CA	ARG	900	31.732	20.569	51.722	1.00	42.23	0
ATOM	5783	CB	ARG	900	31.110	20.432	53.110	1.00	22.01	0
ATOM	5784	CG	ARG	900	30.578	21.718	53.694	1.00	22.01	0
ATOM	5785	CD	ARG	900	30.080	21.488	55.120	1.00	22.01	0
ATOM	5786	NE	ARG	900	31.005	20.664	55.909	1.00	22.01	0
ATOM	5788	CZ	ARG	900	31.111	20.691	57.237	1.00	22.01	0
ATOM	5789	NH1	ARG	900	30.361	21.512	57.963	1.00	22.01	0
ATOM	5792	NH2	ARG	900	31.957	19.865	57.839	1.00	22.01	0
ATOM	5795	C	ARG	900	33.034	21.365	51.774	1.00	42.23	0
ATOM	5796	O	ARG	900	33.795	21.309	52.735	1.00	22.01	0
ATOM	5797	N	ARG	901	33.284	22.091	50.697	1.00	8.39	0
ATOM	5799	CA	ARG	901	34.490	22.880	50.542	1.00	8.39	0
ATOM	5800	CB	ARG	901	34.793	23.036	49.045	1.00	2.00	0
ATOM	5801	CG	ARG	901	34.504	21.810	48.186	1.00	2.00	0
ATOM	5802	CD	ARG	901	34.584	22.175	46.699	1.00	2.00	0
ATOM	5803	NE	ARG	901	34.278	21.012	45.863	1.00	2.00	0
ATOM	5805	CZ	ARG	901	35.190	20.195	45.327	1.00	2.00	0
ATOM	5806	NH1	ARG	901	36.498	20.416	45.509	1.00	2.00	0
ATOM	5809	NH2	ARG	901	34.791	19.114	44.649	1.00	2.00	0
ATOM	5812	C	ARG	901	34.327	24.259	51.158	1.00	8.39	0
ATOM	5813	O	ARG	901	33.241	24.629	51.607	1.00	2.00	0
ATOM	5814	N	VAL	902	35.393	25.005	51.149	1.00	2.00	0
ATOM	5816	CA	VAL	902	35.425	26.384	51.650	1.00	2.00	0
ATOM	5817	CB	VAL	902	36.880	26.814	51.869	1.00	12.90	0
ATOM	5818	CG1	VAL	902	37.039	28.332	51.992	1.00	12.90	0
ATOM	5819	CG2	VAL	902	37.492	26.219	53.139	1.00	12.90	0
ATOM	5820	C	VAL	902	34.782	27.324	50.627	1.00	2.00	0
ATOM	5821	O	VAL	902	34.737	27.031	49.435	1.00	12.90	0
ATOM	5822	N	SER	903	34.288	28.438	51.120	1.00	2.00	0
ATOM	5824	CA	SER	903	33.673	29.487	50.271	1.00	2.00	0
ATOM	5825	CB	SER	903	32.173	29.205	50.008	1.00	2.00	0
ATOM	5826	OG	SER	903	31.477	28.917	51.209	1.00	2.00	0
ATOM	5828	C	SER	903	33.871	30.814	50.991	1.00	2.00	0
ATOM	5829	O	SER	903	34.386	30.866	52.115	1.00	2.00	0
ATOM	5830	N	PHE	904	33.482	31.903	50.376	1.00	2.00	0
ATOM	5832	CA	PHE	904	33.683	33.188	51.034	1.00	2.00	0
ATOM	5833	CB	PHE	904	34.894	33.898	50.455	1.00	17.14	0
ATOM	5834	CG	PHE	904	36.184	33.109	50.672	1.00	17.14	0
ATOM	5835	CD1	PHE	904	36.511	32.067	49.805	1.00	17.14	0
ATOM	5836	CD2	PHE	904	37.034	33.426	51.738	1.00	17.14	0
ATOM	5837	CE1	PHE	904	37.690	31.343	49.994	1.00	17.14	0
ATOM	5838	CE2	PHE	904	38.216	32.704	51.927	1.00	17.14	0
ATOM	5839	CZ	PHE	904	38.544	31.662	51.054	1.00	17.14	0
ATOM	5840	C	PHE	904	32.491	34.080	50.894	1.00	2.00	0
ATOM	5841	O	PHE	904	31.716	33.994	49.926	1.00	17.14	0
ATOM	5842	N	ALA	905	32.386	34.912	51.874	1.00	70.83	0
ATOM	5844	CA	ALA	905	31.311	35.857	51.949	1.00	69.99	0
ATOM	5845	CB	ALA	905	30.042	35.128	52.370	1.00	2.00	0
ATOM	5846	C	ALA	905	31.646	36.940	52.962	1.00	69.85	0
ATOM	5847	O	ALA	905	30.981	37.068	53.993	1.00	2.00	0
ATOM	5848	N	ALA	907	37.374	34.312	47.285	1.00	23.39	0
ATOM	5850	CA	ALA	907	36.215	33.651	46.695	1.00	23.39	0
ATOM	5851	CB	ALA	907	35.317	34.681	46.008	1.00	41.64	0
ATOM	5852	C	ALA	907	36.637	32.568	45.699	1.00	23.39	0
ATOM	5853	O	ALA	907	35.850	31.680	45.370	1.00	41.64	0
ATOM	5854	N	ALA	908	37.875	32.643	45.215	1.00	83.90	0
ATOM	5856	CA	ALA	908	38.378	31.663	44.253	1.00	83.90	0
ATOM	5857	CB	ALA	908	39.439	32.296	43.337	1.00	22.84	0
ATOM	5858	C	ALA	908	38.961	30.466	44.992	1.00	83.90	0
ATOM	5859	O	ALA	908	38.459	30.074	46.046	1.00	22.84	0
ATOM	5860	OW	WAT	1	62.869	37.982	63.341	1.00	20.00	0
ATOM	5863	OW	WAT	103	57.039	39.062	61.228	1.00	20.00	0
ATOM	5866	OW	WAT	101	7.257	66.194	118.365	1.00	20.00	0
ATOM	5869	OW	WAT	2	12.341	60.209	123.464	1.00	20.00	0
ATOM	5872	OW	WAT	3	10.655	60.748	120.833	1.00	20.00	0

ATOM	5875	OW	WAT	104	55.432	36.306	63.901	1.00	20.00	0
ATOM	5878	OW	WAT	102	56.782	40.457	58.333	1.00	20.00	0
ATOM	5881	OW	WAT	4	5.787	57.856	118.686	1.00	20.00	0
ATOM	5884	OW	WAT	105	54.382	39.155	63.734	1.00	20.00	0
ATOM	5887	OW	WAT	5	8.964	57.595	118.151	1.00	20.00	0
ATOM	5890	OW	WAT	106	38.565	47.423	74.959	1.00	20.00	0
ATOM	5893	OW	WAT	6	16.086	42.169	105.289	1.00	20.00	0
ATOM	5896	OW	WAT	107	31.158	26.414	51.913	1.00	20.00	0
ATOM	5899	OW	WAT	7	-0.781	32.787	131.574	1.00	20.00	0
ATOM	5902	MN	MN2	430	4.422	59.061	119.360	1.00	15.61	0
ATOM	5903	MN	MN2	431	7.458	57.875	117.661	1.00	16.53	0
ATOM	5904	MN	MN2	930	56.038	34.500	63.727	1.00	16.67	0
ATOM	5905	MN	MN2	931	54.402	37.798	64.756	1.00	15.40	0
ATOM	5906	S	SO4	801	57.551	37.278	64.009	1.00	37.87	0
ATOM	5907	O1	SO4	801	57.600	35.852	63.897	1.00	42.46	0
ATOM	5908	O2	SO4	801	58.690	37.740	64.722	1.00	42.01	0
ATOM	5909	O3	SO4	801	56.355	37.648	64.705	1.00	45.08	0
ATOM	5910	O4	SO4	801	57.520	37.854	62.725	1.00	41.40	0
ATOM	5911	S	SO4	800	6.866	60.776	118.643	1.00	37.87	0
ATOM	5912	O1	SO4	800	7.710	60.635	119.773	1.00	42.46	0
ATOM	5913	O2	SO4	800	7.044	62.063	118.053	1.00	42.01	0
ATOM	5914	O3	SO4	800	5.496	60.612	119.046	1.00	45.08	0
ATOM	5915	O4	SO4	800	7.194	59.728	117.703	1.00	41.40	0

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CLAIMS

1. A method of identifying a compound which modulates the interaction between a PP1c and a regulatory subunit thereof, the method comprising determining whether a compound enhances or disrupts the interaction between (a) a PP1c or a fragment, variant, derivative or fusion thereof or a fusion of a fragment, variant or derivative and (b) a regulatory subunit which is able to bind to PP1c or a PP1c-binding fragment, variant, derivative or fusion of said subunit or a fusion of said fragment, variant or derivative.

2. A method of identifying a compound which mimics the effect of a regulatory subunit of PP1c, the method comprising contacting said compound with PP1c and determining whether, in the presence of the compound, PP1c adopts the function of properties of a PP1c in the presence of a given regulatory subunit.

3. A method according to Claim 1 or 2 wherein said regulatory subunit of PP1c is any one of M_{110}, G_L, G_M, M-complexes, p53 BP2, sds22, NIPPI, L5, Inhibitor-1, Inhibitor-2, or DARPP.

4. A method according to Claim 3 wherein the regulatory subunit of PP1c is any one of M_{110}, G_L, G_M, M-complexes or p53BP2.

5. A method according to Claim 4 wherein the regulatory subunit of PP1c is M_{110} or G_M.

6. A method according to Claim 1 wherein the fragment of a regulatory subunit which is able to bind to PP1c is any of the peptides [G63-T93], [G63-N75], [E2-P243], [E2-D118], and peptide 63-80 of G_M or

functional equivalents thereof or peptides comprising said peptide sequences provided that they are not the complete G_M regulatory subunit.

7. A method according to Claim 1 wherein the fragment of a regulatory subunit which is able to bind to PP1c is any of the peptides [M1-E309], [M1-F38], [M1-A150] or [L24-Y496] of M_{110} or functional equivalents thereof or peptides comprising said peptide sequences provided that they are not the complete M_{110} regulatory subunit.

8. A method according to Claim 1 wherein the PP1c-binding fragment, variant or derivative of said regulatory subunit or a fusion of said fragment, variant or derivative comprises the consensus peptide sequence Arg/Lys-Val/Ile-Xaa-Phe wherein Xaa is any amino acid.

9. A method according to Claim 8 wherein the PP1c-binding fragment, variant or derivative comprises, in addition to the said consensus peptide sequence, at least one basic residue in the four residues N-terminal of the consensus peptide sequence.

10. A method according to Claim 8 wherein in the consensus peptide sequence Xaa is not Asp or Glu or a large hydrophobic residue.

11. A method according to Claim 8 wherein the PP1c-binding fragment is a fragment of a regulatory subunit comprising the said consensus peptide sequence.

12. A method according to Claim 10 wherein the PP1c-binding fragment is a fragment of any of the M_{110}, G_L, G_M, M-complexes, p53BP2, sds22, NIPPI, L5, Inhibitor-1, Inhibitor-2 or DARPP regulatory subunits comprising said consensus sequence.

13. A method according to any one of the preceding claims wherein the compound binds to a PP1c.

14. A method according to Claim 1 wherein the compound binds to a regulatory subunit of PP1c.

15. A compound identifiable by the method of any one of Claims 1 to 14.

16. A compound which modulates the interaction between a PP1c and a regulatory subunit thereof said compound comprising any of the peptides [G63-T93], [G63-N75], [E2-P243], [E2-D118], and peptide 63 to 80 of G_M or functional equivalents or said compound comprising any of the peptides [M1-E309], [M1-F38], [M1-A150] or [L24-Y496] of M_{110} or functional equivalents thereof or said compound comprising the consensus peptide sequence Arg/Lys-Val/Ile-Xaa-Phe wherein Xaa is any naturally occurring amino acid or functional equivalents thereof, provided that the said compound is not a complete regulatory subunit of PP1c.

17. A compound according to Claim 16 consisting of the peptides [G63-T93], [G63-N75], [E2-P243], [E2-D118], or peptide 63 to 80 of G_M or functional equivalents thereof or consisting of the peptides [M1-E309], [M1-F38], [M1-A150] or [L24-Y496] of M_{110} or functional equivalents thereof.

18. A peptide capable of binding a PP1c and which affects the ability of PP1c to bind to a particular target and/or affects the regulation of PP1c activity, or a functional equivalent thereof.

19. A method of identifying a compound which modulates the interaction

between a PP1c and a regulatory subunit thereof, or binds PP1c or mimics the effect of a regulatory subunit, the method comprising selecting a compound which is capable of adopting the same or substantially the same conformation as a peptide bound to the regulatory subunit-binding site of PP1c or the same or substantially the same conformation as the portion of PP1c which binds to said peptide.

20. A method according to Claim 19 wherein said peptide comprises the consensus peptide sequence Arg/Lys-Val/Ile-Xaa-Phe wherein Xaa is any amino acid.

21. A method according to Claim 20 wherein said peptide consists of residues 63 to 75 of G_M.

22. A method according to Claim 21 wherein the conformation of the said peptide and the conformation of the said portion of PP1c is as defined by reference to the coordinates in Table A.

23. A compound identifiable by the method of any one of Claims 19 to 22.

24. A compound according to any one of Claims 15 to 18 or 23 for use in medicine.

25. A pharmaceutical composition comprising a compound according to any one of Claims 15 to 18 or 23 and a pharmaceutically acceptable carrier.

26. A method of affecting cellular metabolism or function, the method comprising administering to a cell (a) a compound which modulates the interaction between a PP1c and a regulatory subunit thereof or (b) a compound which mimics the effect of a regulatory subunit of PP1c or

(c) a peptide capable of binding a PP1c and which affects the ability of PP1c to bind to a particular target and/or affects the regulation of PP1c activity, or a functional equivalent thereof.

27. A method according to Claim 26 wherein any one or more of the peptides [G63-T93], [G63-N75], [E2-P243], [E2-D118], and peptide 63-80 of G_M or functional equivalents thereof or peptides comprising said peptide sequences are administered.

28. A method according to Claim 26 wherein any one or more of the peptides [M1-E309], [M1-F38], [M1-A150] or [L24-Y496] of M_{110} or functional equivalents thereof or peptides comprising said peptide sequences are administered.

29. A method according to Claim 26 wherein a compound according to any one of Claims 15 to 18 or 23 are administered to the cell.

30. A method according to any one of Claims 26 to 29 wherein the cell is in a mammalian body.

31. A method of treating a patient in need of modulation of PP1c activity or function the method comprising administering to the patient an effective amount of a compound which modulates the interaction between a PP1c and a regulatory subunit thereof or (b) a compound which mimics the effect of a regulatory subunit of PP1c or (c) a peptide capable of binding a PP1c and which affects the ability of PP1c to bind to a particular target and/or affects the regulation of PP1c activity, or a functional equivalent thereof.

32. Use of peptides derived from targeting subunits of PP1c, functional

equivalents or portions thereof to affect cellular metabolism.

33. A method of treatment of a mammal said method comprising altering levels of peptides derived from a targeting subunit of PP1c, functional equivalents or portions thereof to an extent that cellular metabolism or function is affected.

34. A PP1c-regulating subunit that is modified so that it cannot interact with PP1c.

35. A PP1c-regulator subunit according to Claim 34 wherein the consensus peptide sequence Arg/Lys-Val/Ile-Xaa-Phe is missing or modified.

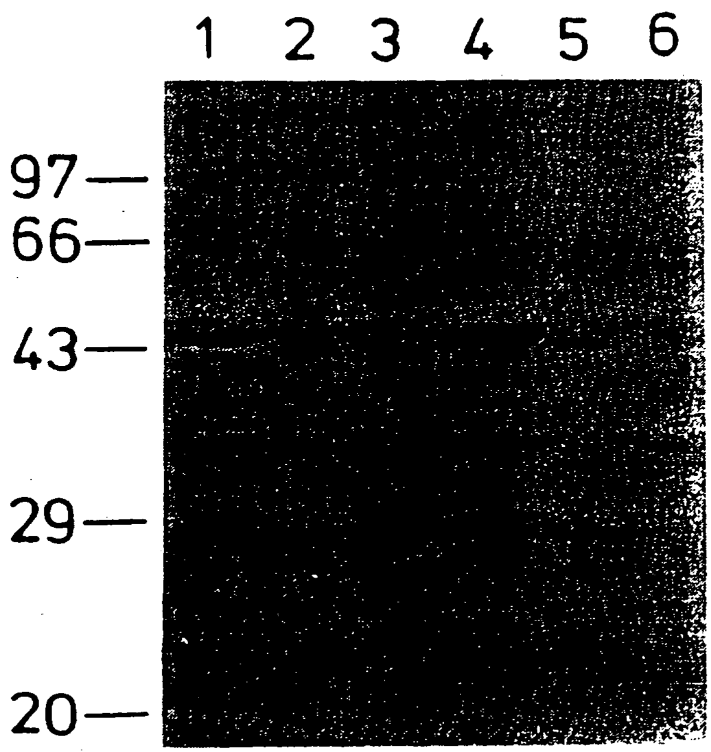


Fig. 1

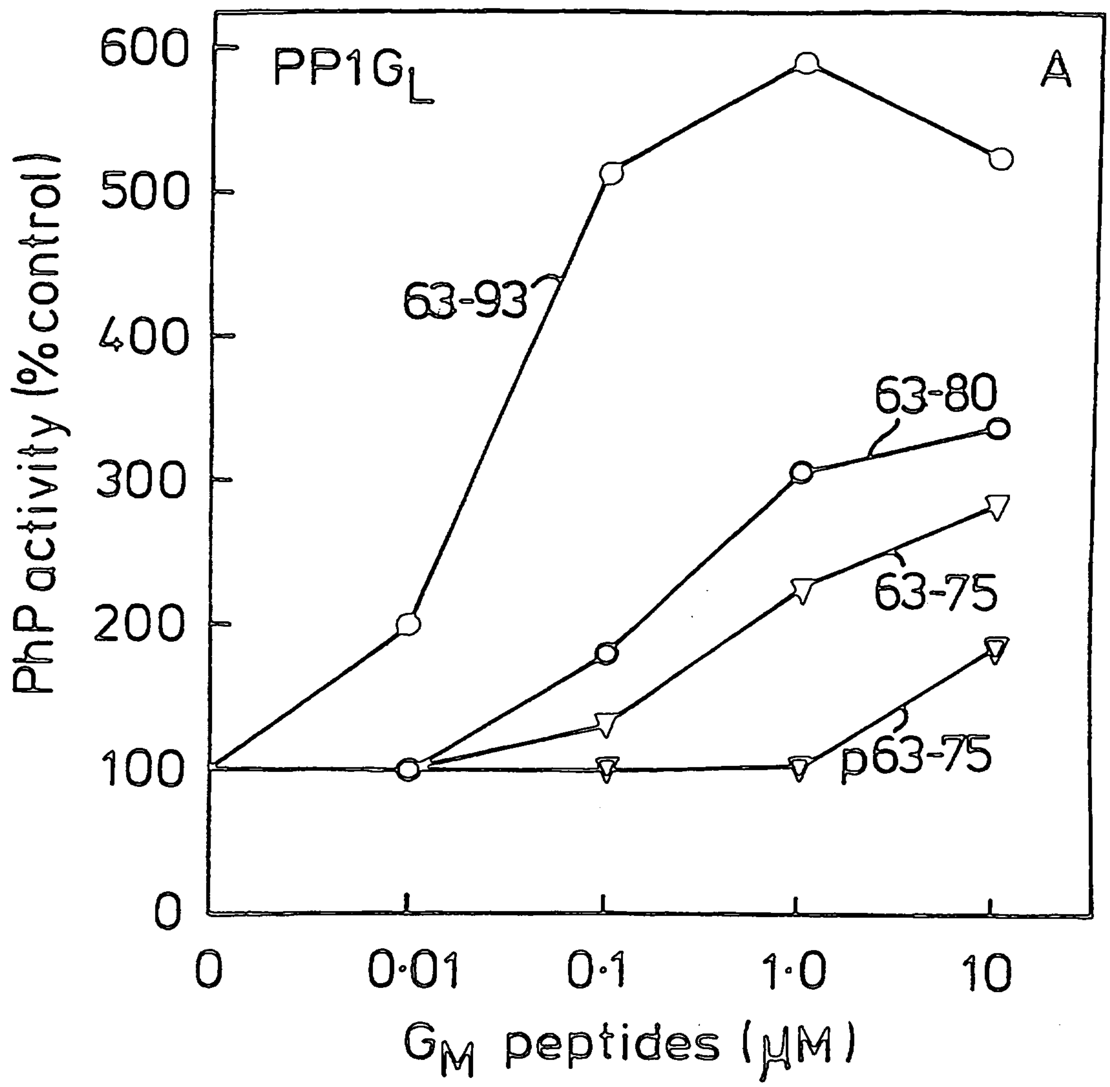

PP1GL
A
PhP activity (%control)
600
500
400
300
200
100
0
63-93
63-80
63-75
p63-75
0
0·01
0·1
1·0
10
GM peptides (µM)

Fig. 2

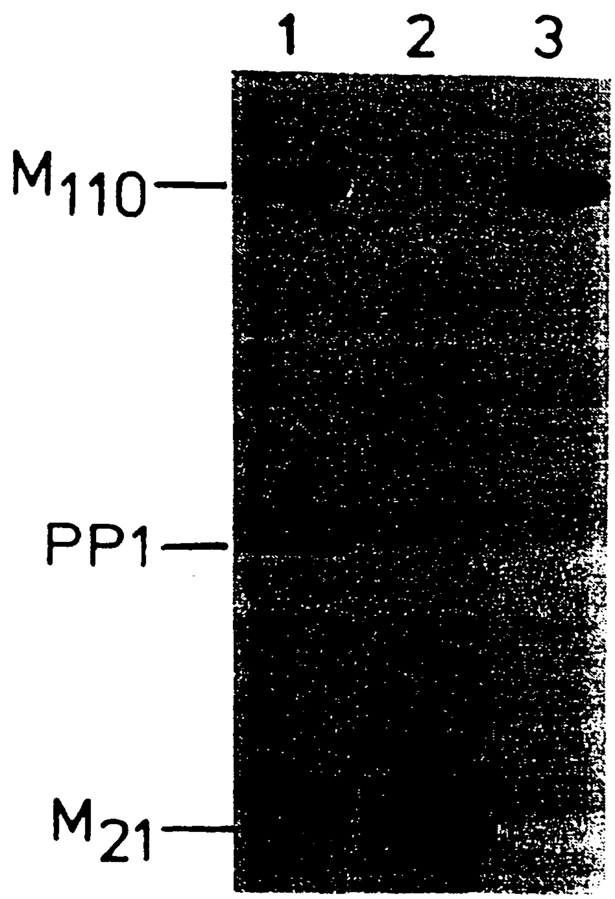


Fig. 3A

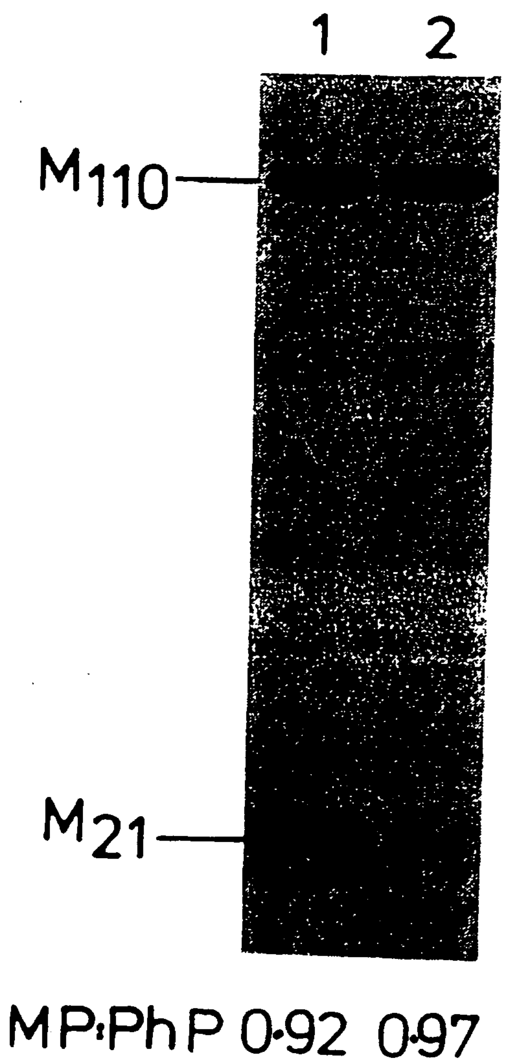


Fig 3B

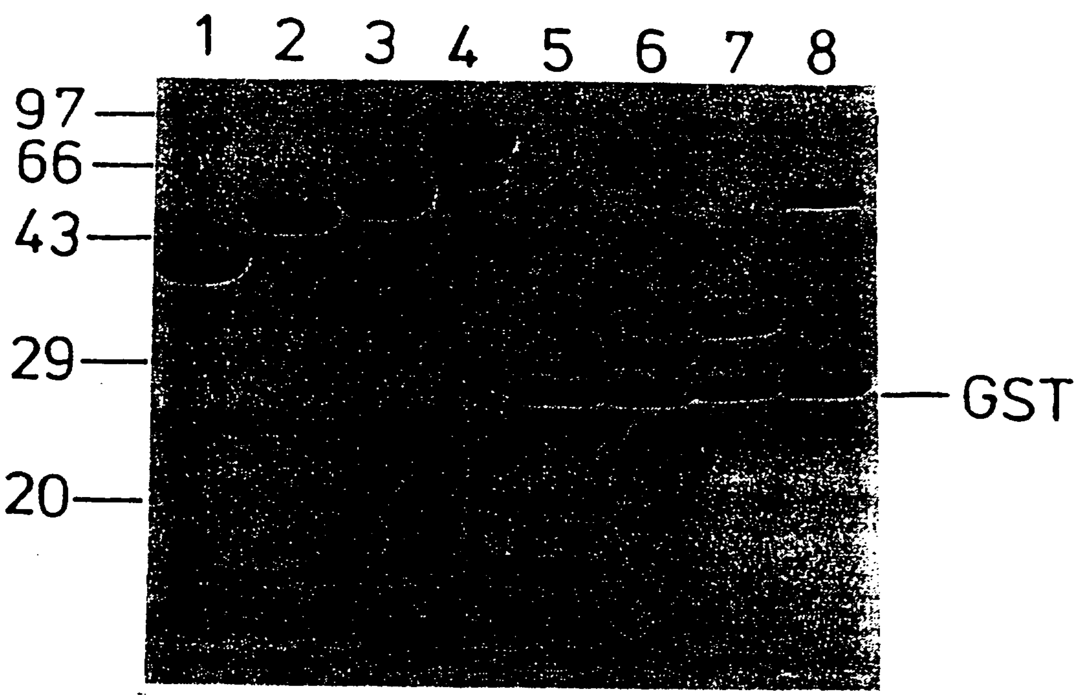


Fig. 4

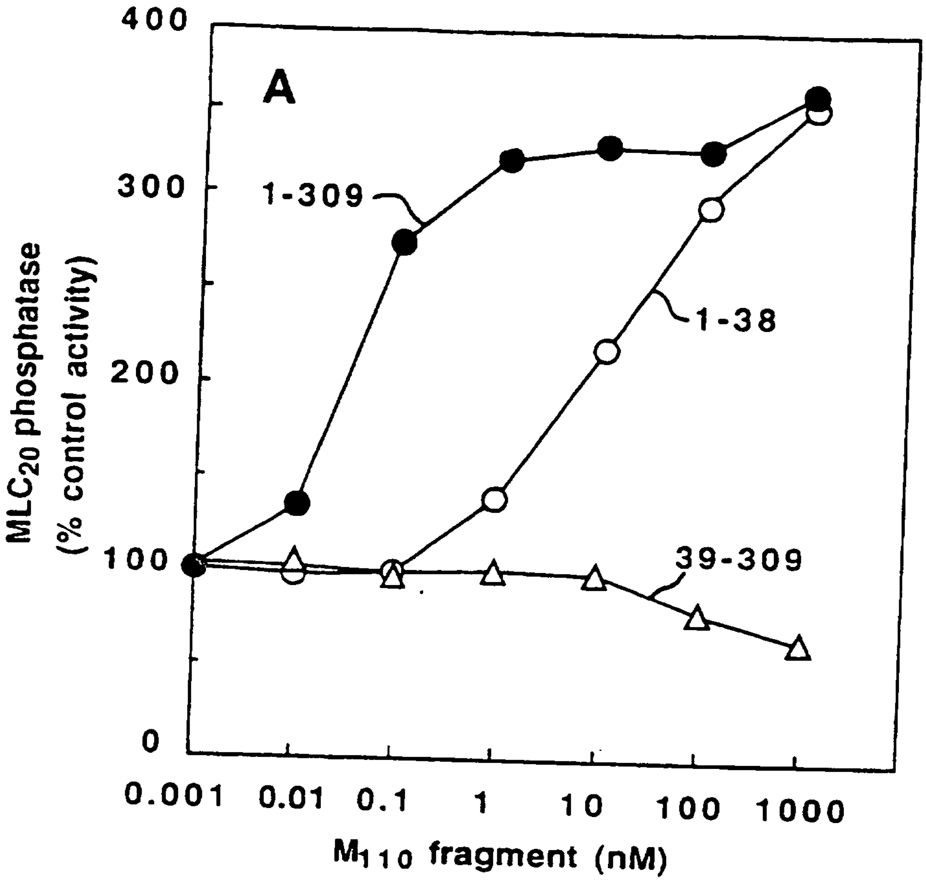

A
400
300
200
100
0
MLC20 phosphatase
(% control activity)
1-309
1-38
39-309
0.001 0.01 0.1 1 10 100 1000
M110 fragment (nM)

Fig. 5A

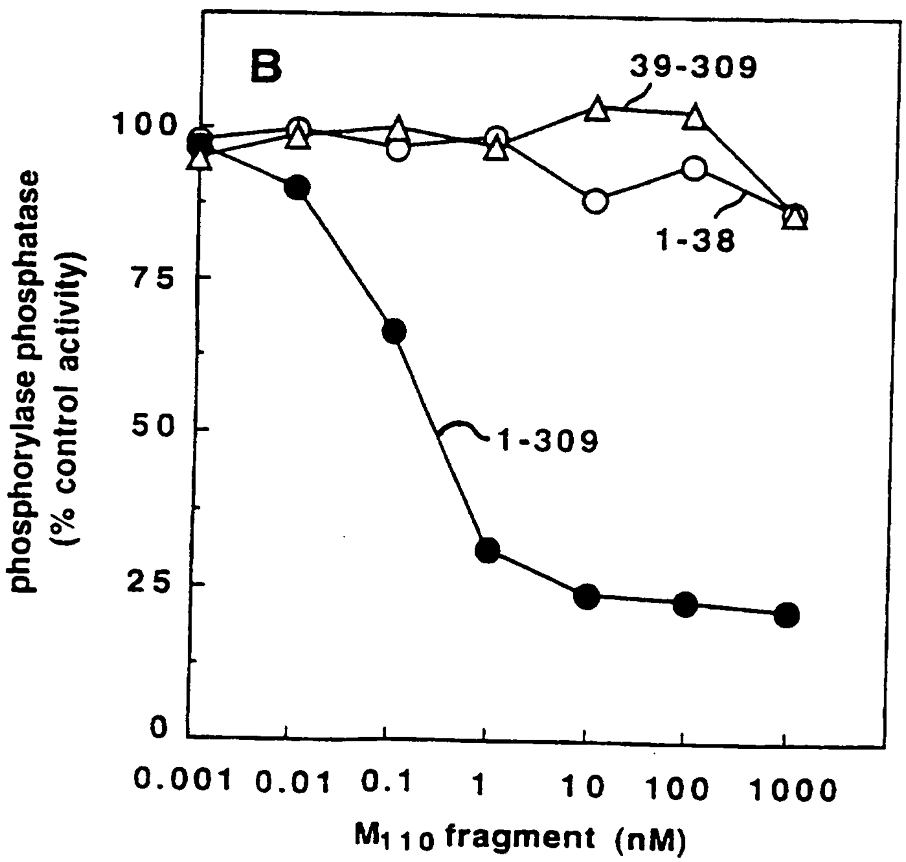

B
100
75
50
25
0
phosphorylase phosphatase
(% control activity)
39-309
1-38
1-309
0.001 0.01 0.1 1 10 100 1000
M110 fragment (nM)

Fig. 5B

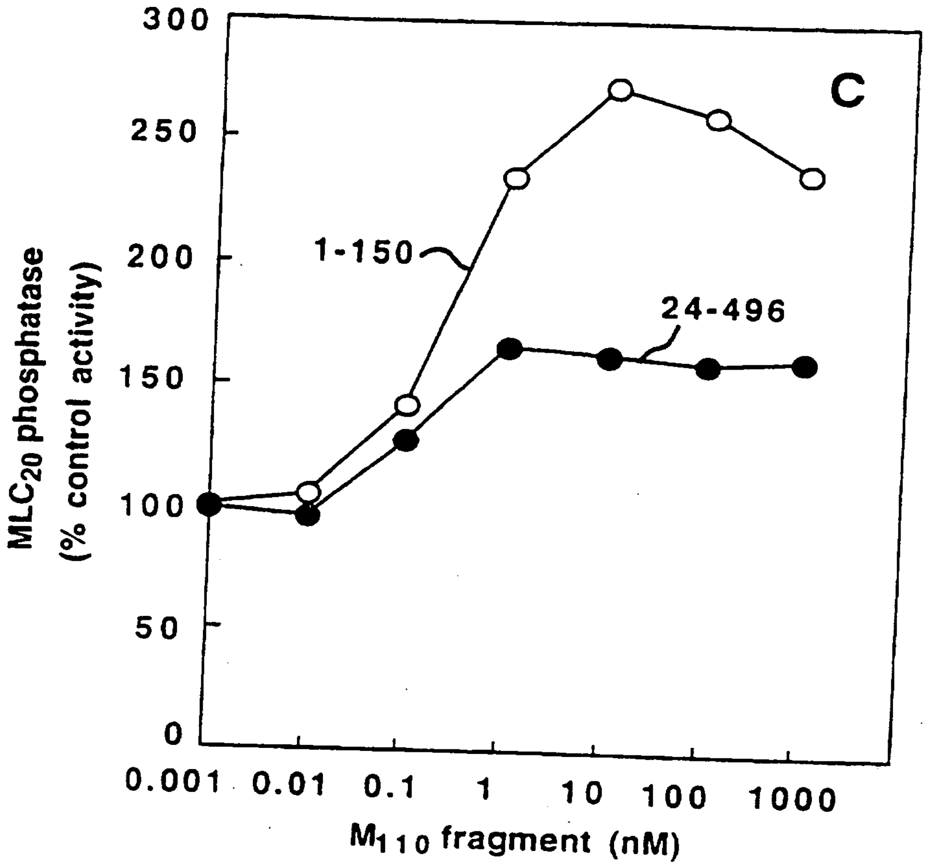

300
250
200
150
100
50
0
C
1-150
24-496
MLC20 phosphatase
(% control activity)
0.001 0.01 0.1 1 10 100 1000
M110 fragment (nM)

Fig. 5C

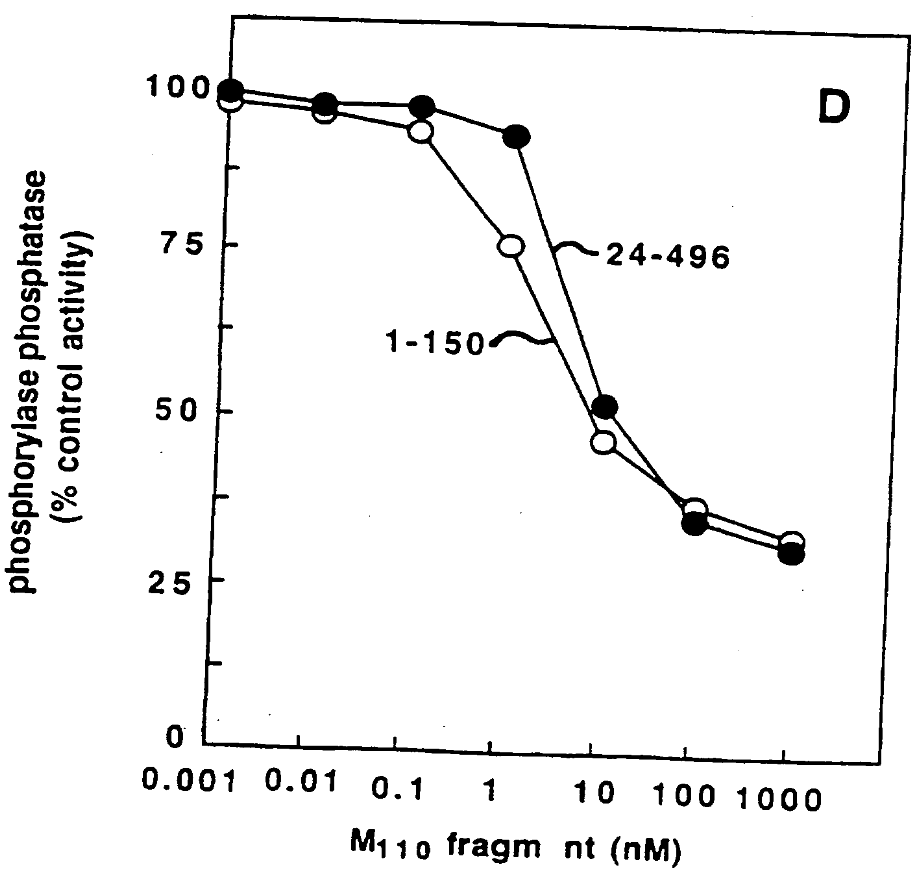
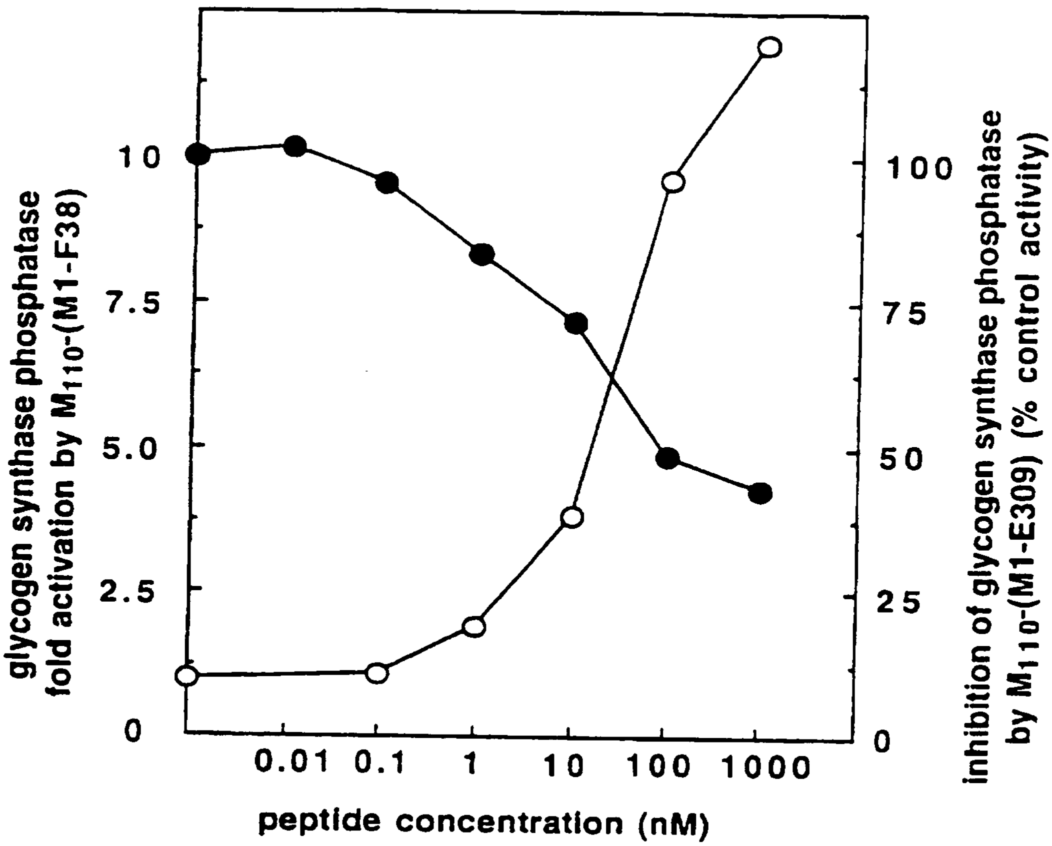

100
75
50
25
0
D
24-496
1-150
phosphorylase phosphatase
(% control activity)
0.001 0.01 0.1 1 10 100 1000
M110 fragm nt (nM)

Fig. 5D



glycogen synthase phosphatase fold activation by M_{110}-(M1-F38)
10
7.5
5.0
2.5
0
0.01 0.1 1 10 100 1000
peptide concentration (nM)
inhibition of glycogen synthase phosphatase by M_{110}-(M1-E309) (% control activity)
100
75
50
25
0

Fig 6

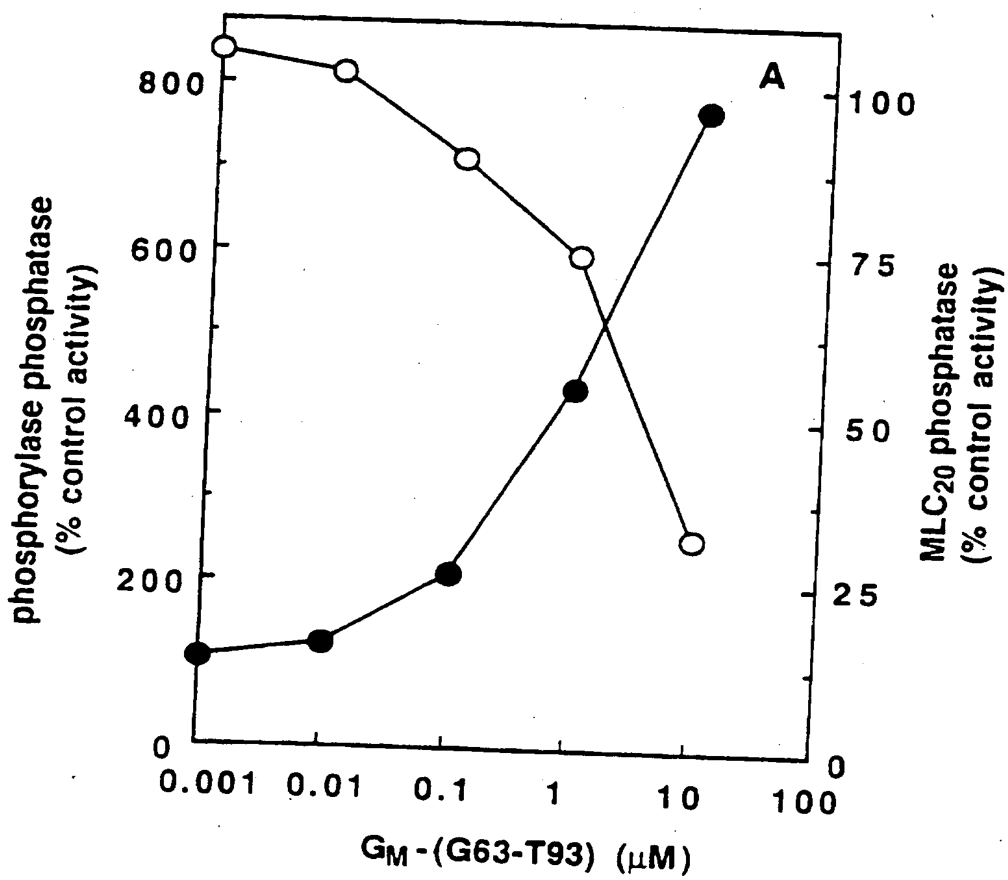

A
800
600
400
200
0
100
75
50
25
0
0.001
0.01
0.1
1
10
100
phosphorylase phosphatase
(% control activity)
MLC_{20} phosphatase
(% control activity)
G_M-(G63-T93) (μM)

Fig 7A

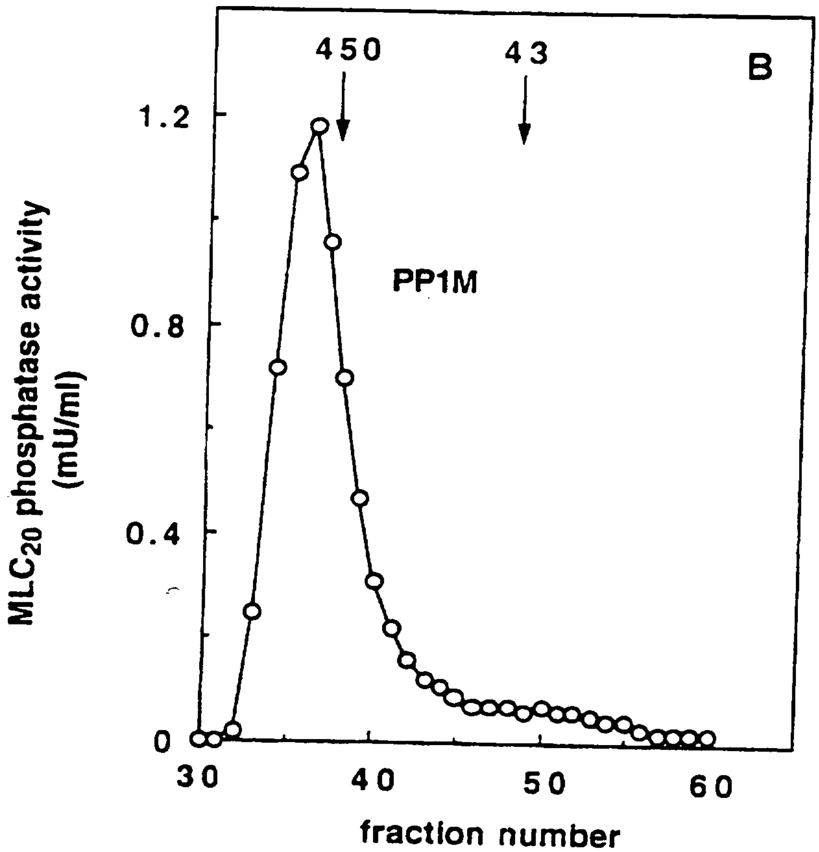

450
43
B
PP1M
MLC20 phosphatase activity (mU/ml)
1.2
0.8
0.4
0
30
40
50
60
fraction number

Fig. 7B

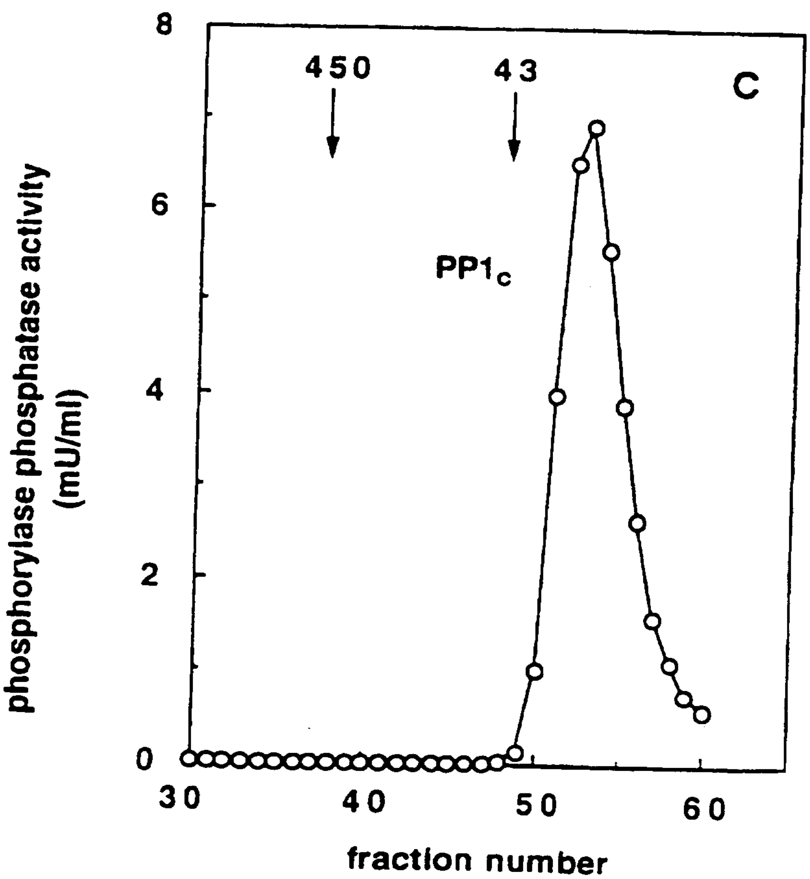

450
43
C
PP1c
phosphorylase phosphatase activity (mU/ml)
8
6
4
2
0
30
40
50
60
fraction number

Fig. 7C

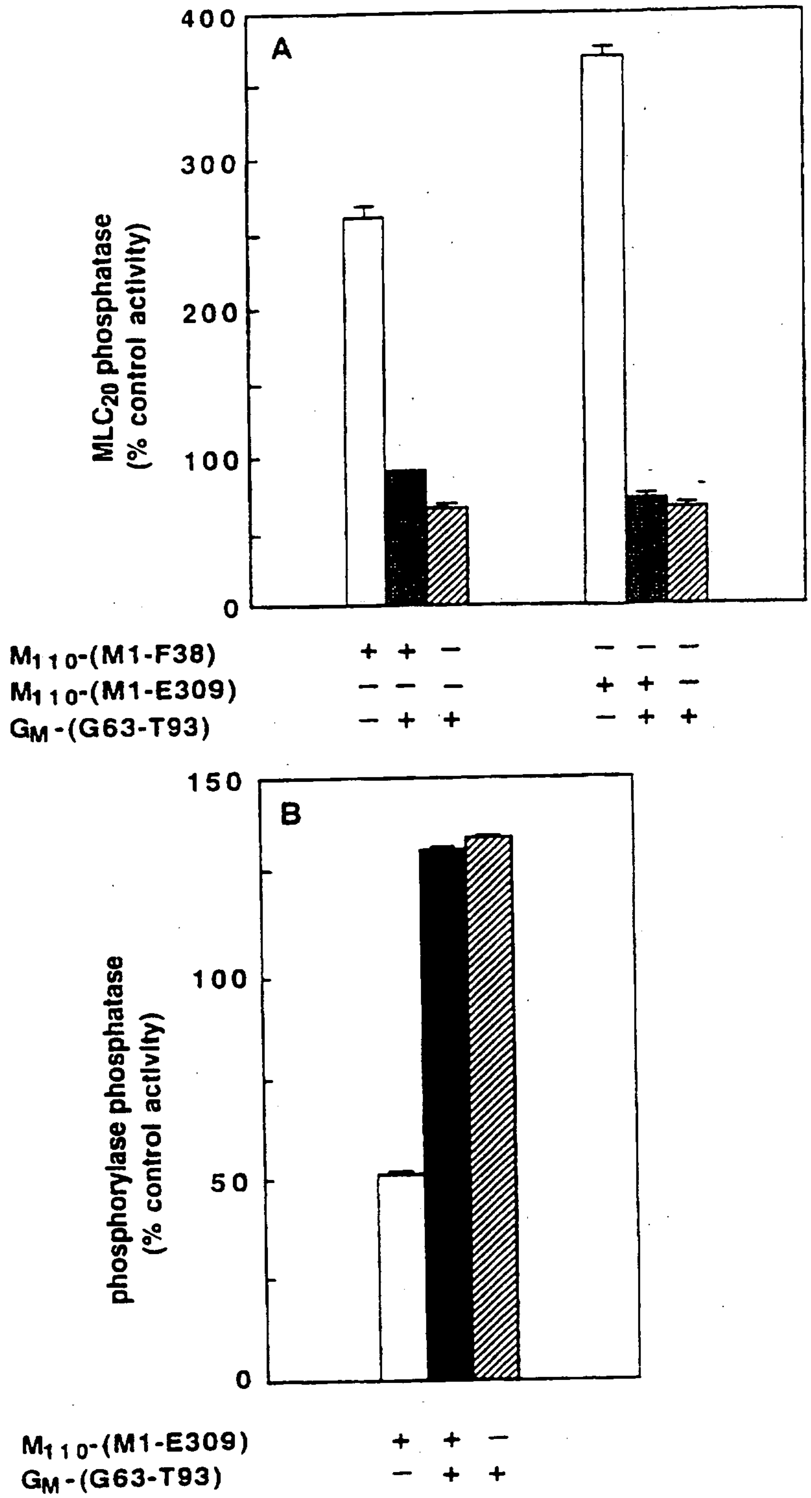
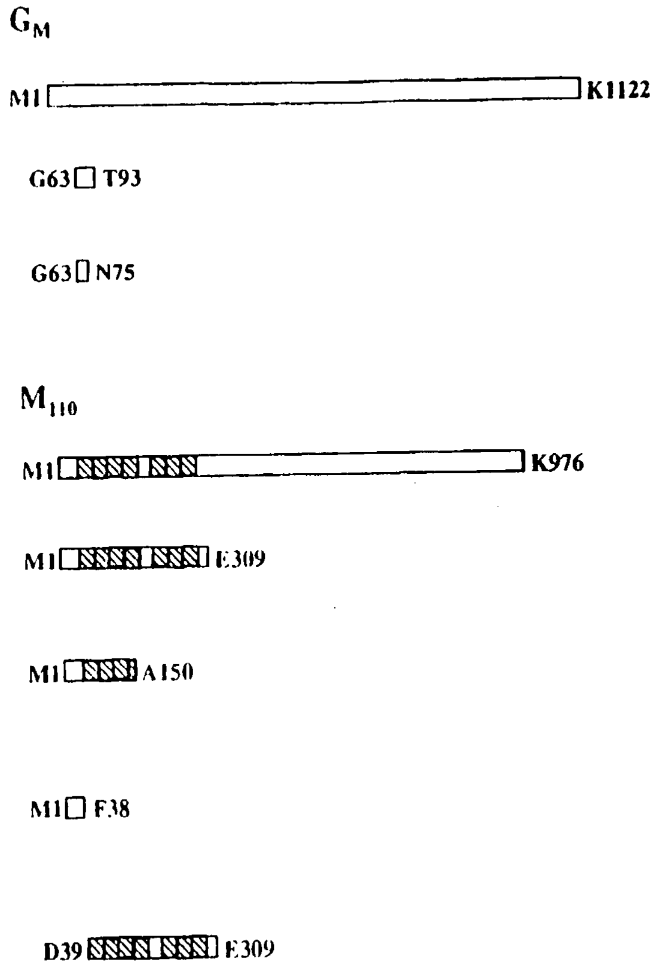

A
MLC20 phosphatase
(% control activity)
400
300
200
100
0
M110-(M1-F38) + + − − − −
M110-(M1-E309) − − − + + −
GM-(G63-T93) − + + − + +
B
phosphorylase phosphatase
(% control activity)
150
100
50
0
M110-(M1-E309) + + −
GM-(G63-T93) − + +

Fig 8



Fragment	Effect of fragment on $PP1G_L$ and/or PP1M activity	Dissociation of $PP1G_L$ and/or PP1M by fragment
G_M M1–K1122		
G63–T93	prevents G_L from suppressing the dephosphorylation of phosphorylase	does not dissociate G_L from $PP1G_L$; displaces M_{110} from PP1M
G63–N75	prevents G_L from suppressing the dephosphorylation of phosphorylase	
M_{110} M1–K976		
M1–E309	stimulates dephosphorylation of MLC_{20} <u>and</u> suppresses dephosphorylation of phosphorylase	displaces G_L from $PP1G_L$
M1–A150	stimulates dephosphorylation of MLC_{20} <u>and</u> suppresses dephosphorylation of phosphorylase	
M1–F38	stimulates dephosphorylation of MLC_{20} but does <u>not</u> suppress the dephosphorylation of phosphorylase	displaces G_L from $PP1G_L$
D39–E309	no effect on PP1C activity	

Fig. 9

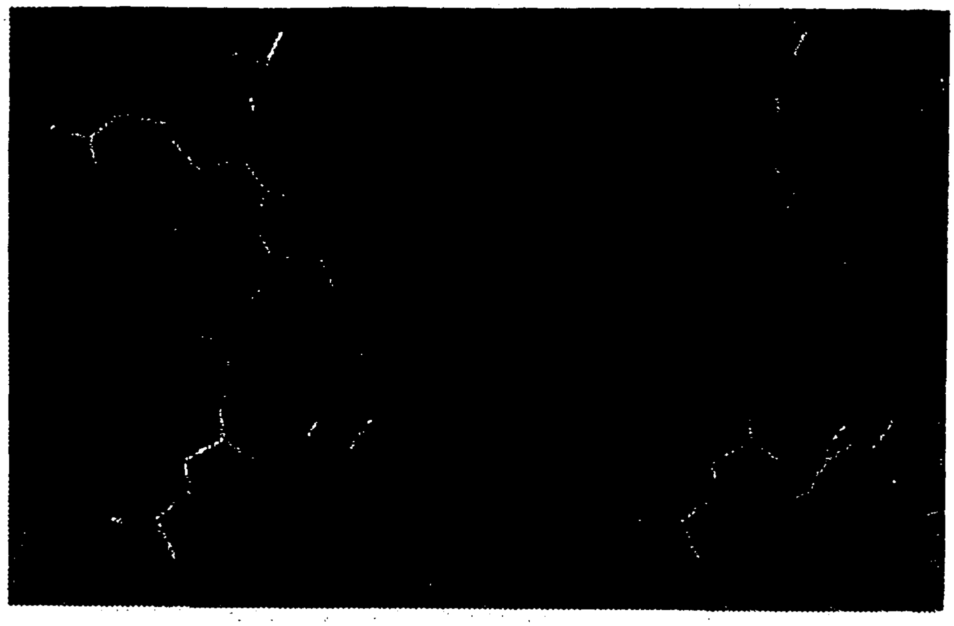


Fig. 10A

Fig 10B

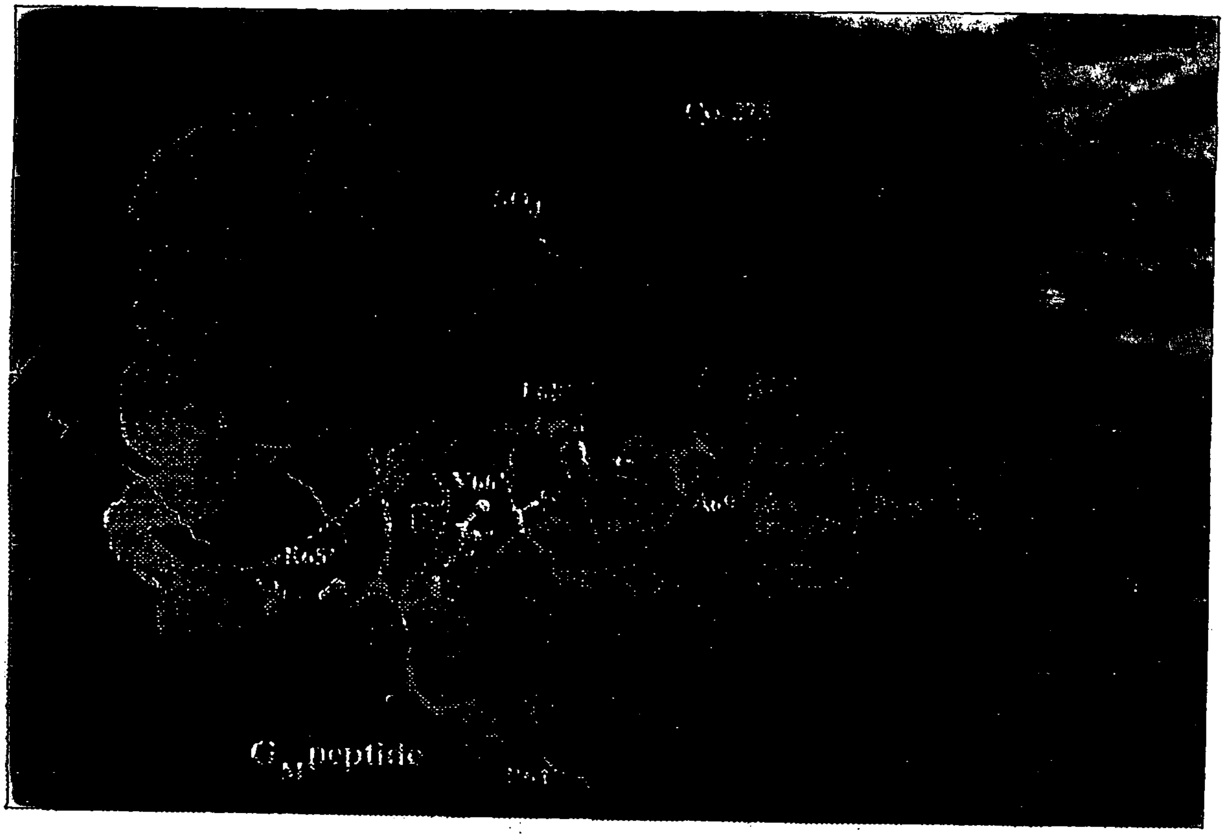


Fig. 11A

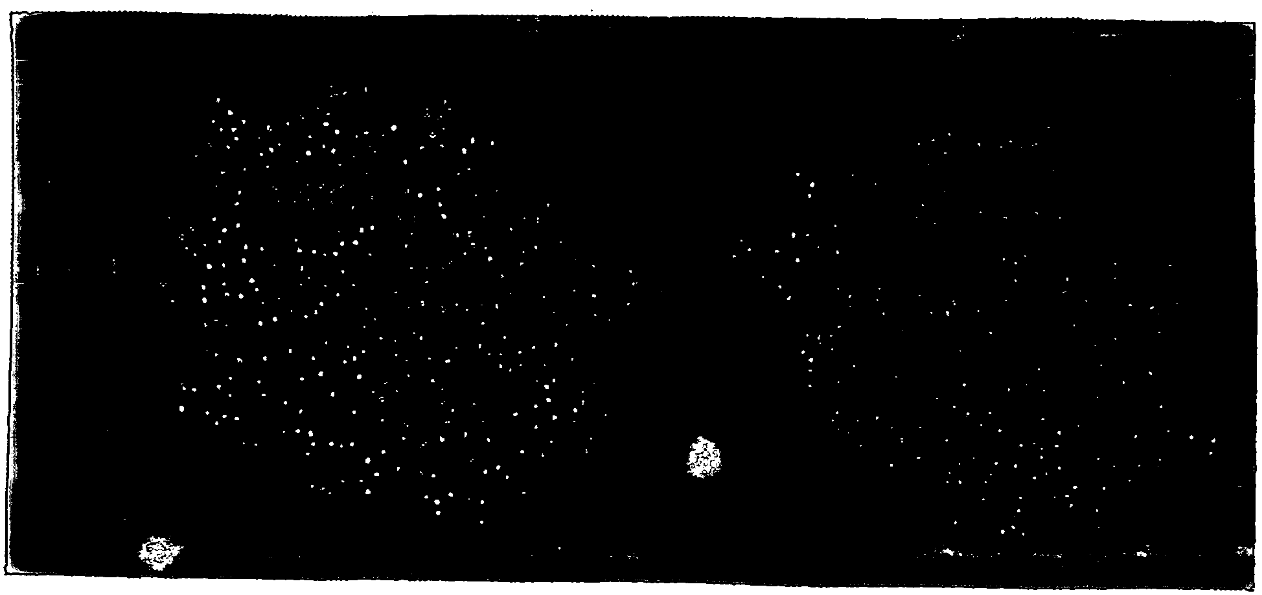


Fig. 11B

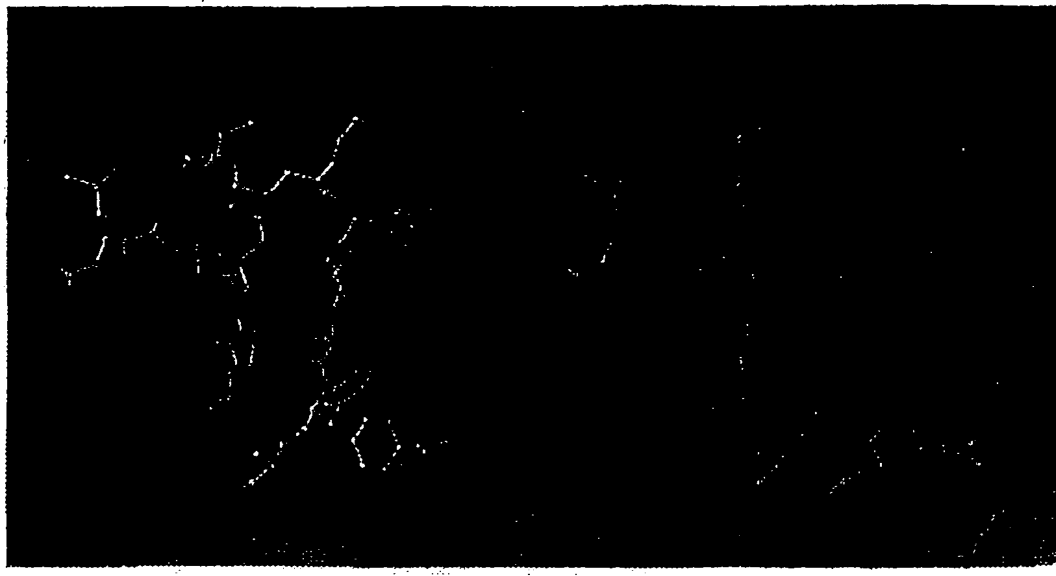


Fig. 11C

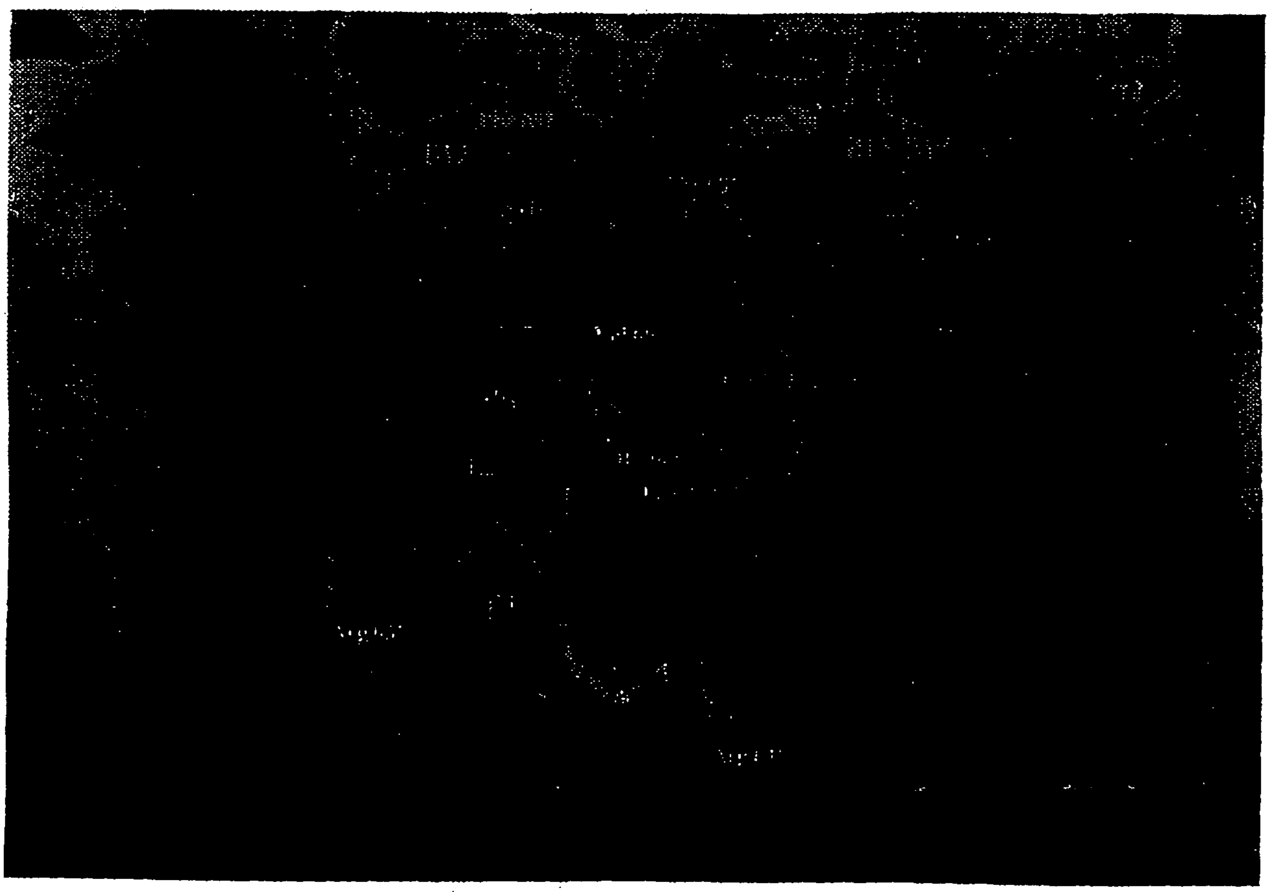


Fig 11E

protein	putative PP1-binding motif	residues
GAC1	S P E **K** N **V** R **F** A I E	66-76
PIG2	S S G **K** S **V** R **F** A A H	50-60
GIP2	I R S **K** S **V** H **F** D Q A	217-227
YIL045W	Q R S **K** S **V** H **F** D R V	193-203
YIL045W	V F V **K** N **I** Y **F** S N A	412-422
REG1	T K N **R** H **I** H **F** N D R	461-471
REG2	P R E **R** H **I** K **F** N D N	164-174
SCD5	F K S **K** K **V** R **F** S E H	270-280
GIP1	L S E **K** F **I** P **F** N N L	180-190
GIP1	K K K **R** C **V** N **F** R N K	441-451
SHP1	K V T **R** E **I** T **F** W K E	232-242

Fig. 12A

protein	Putative PP1-binding motif			residues
GAC1	S P E	K N V R F A	I E	66-76
PIG2	S S G	K S V R F A	A H	50-60
GIP2	I R S	K S V H F D	Q A	217-227
YIL045W	Q R S	K S V H F D	R V	193-203
YIL045W	V F V	K N I Y F S	N A	412-422
REG1	T K N	R H I H F N	D R	461-471
REG2	P R E	R H I K F N	D N	164-174
SCD5	F K S	K K V R F S	E H	270-280
GIP1	W N L	K F I P F N	N L	180-190
GIP1	K K K	R C V N F R	N K	441-451

Fig 12B

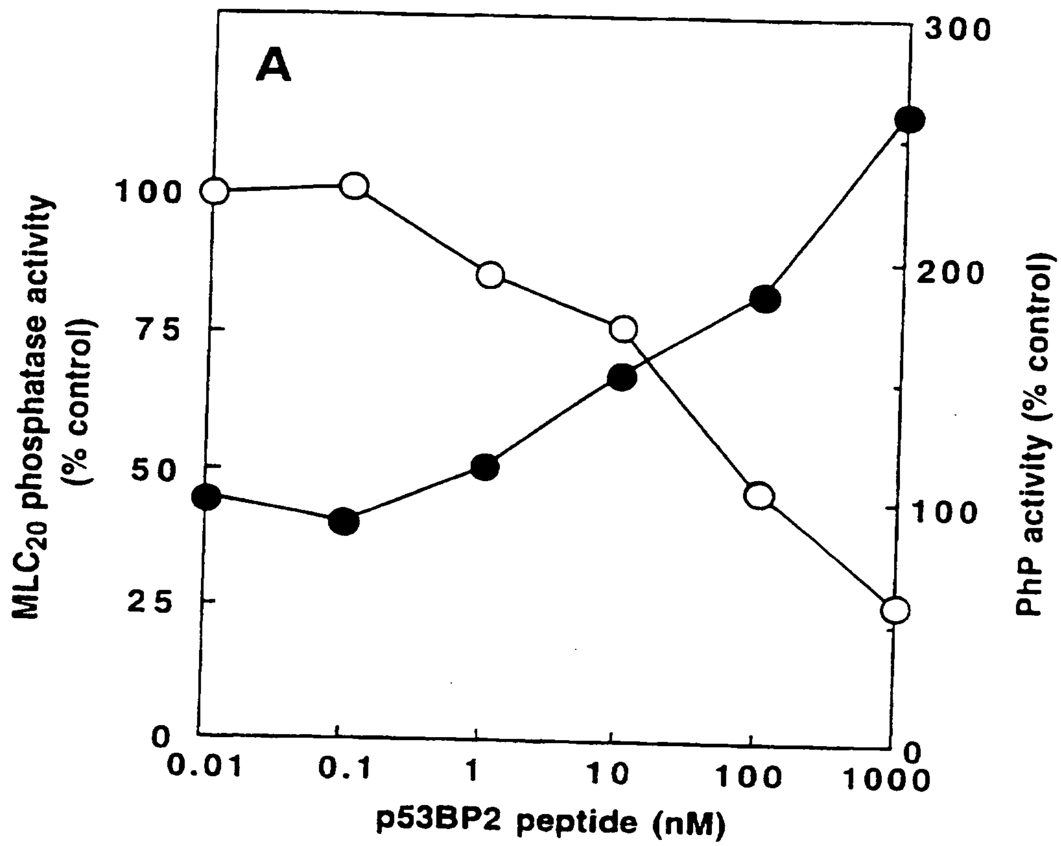

A
MLC20 phosphatase activity (% control)
100
75
50
25
0
PhP activity (% control)
300
200
100
0
0.01
0.1
1
10
100
1000
p53BP2 peptide (nM)

Fig. 13A

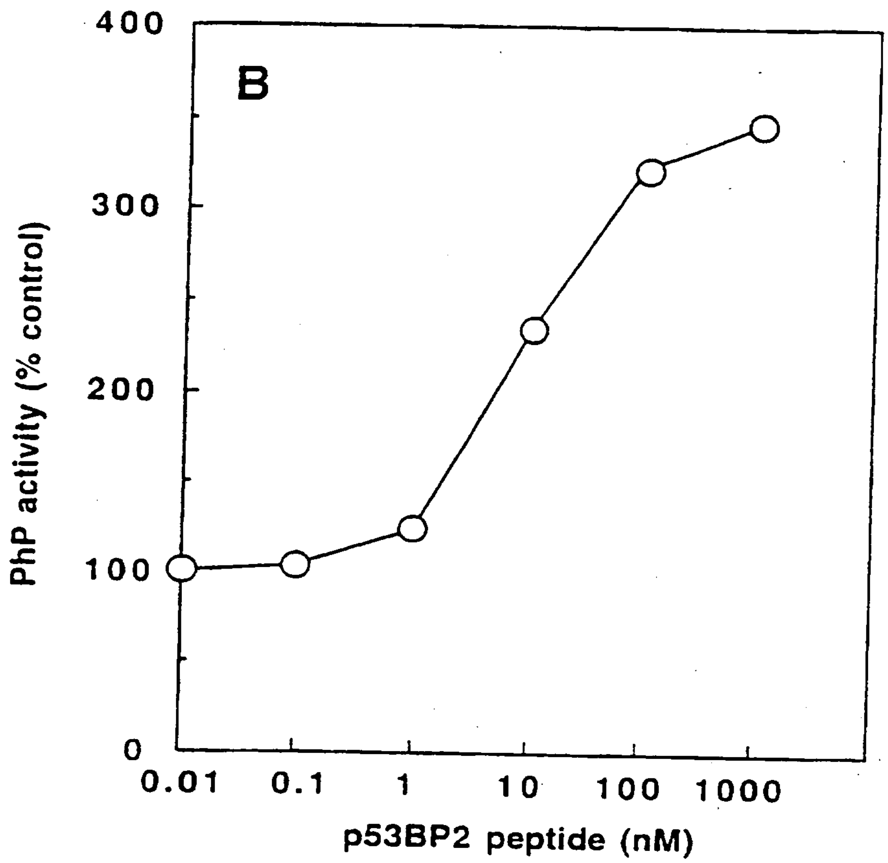

B
400
300
200
100
0
PhP activity (% control)
0.01
0.1
1
10
100
1000
p53BP2 peptide (nM)

Fig 13B

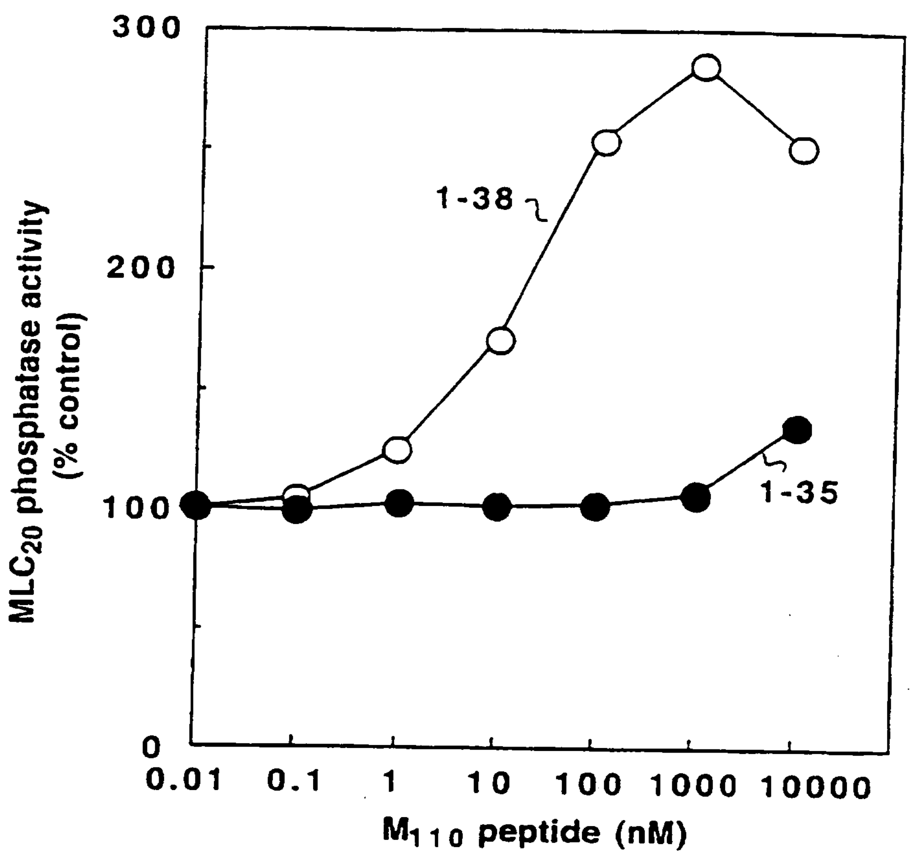

300
200
100
0
MLC20 phosphatase activity
(% control)
1-38
1-35
0.01
0.1
1
10
100
1000
10000
M110 peptide (nM)

Fig 14

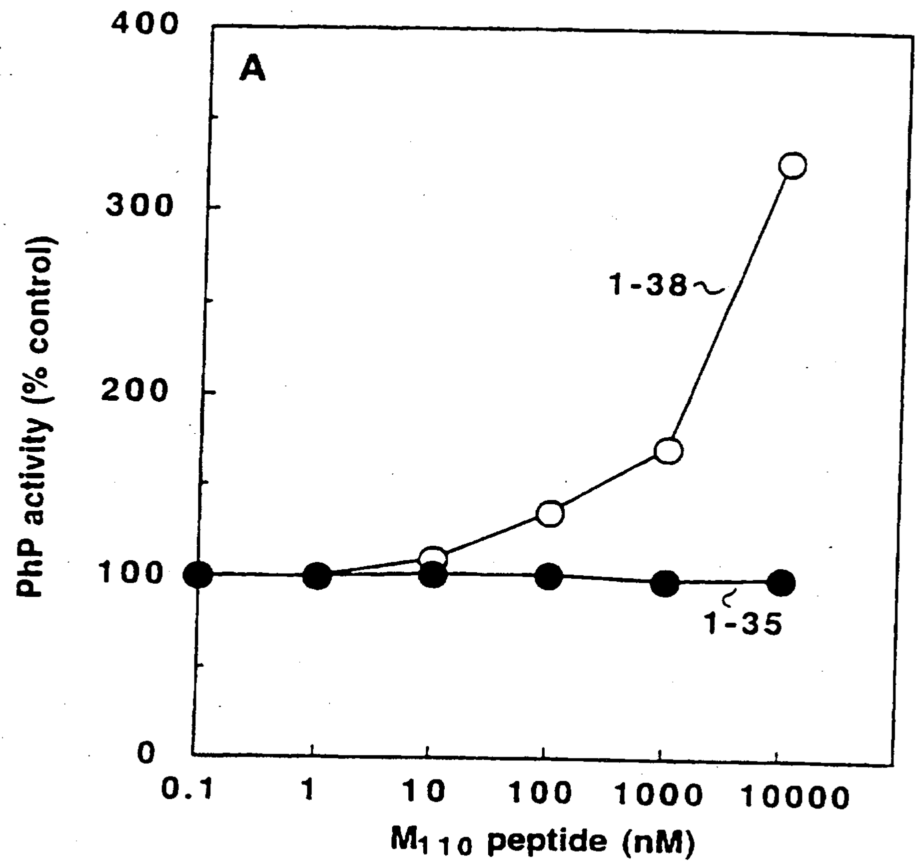

A
PhP activity (% control)
400
300
200
100
0
1-38
1-35
0.1
1
10
100
1000
10000
M110 peptide (nM)

Fig 15A

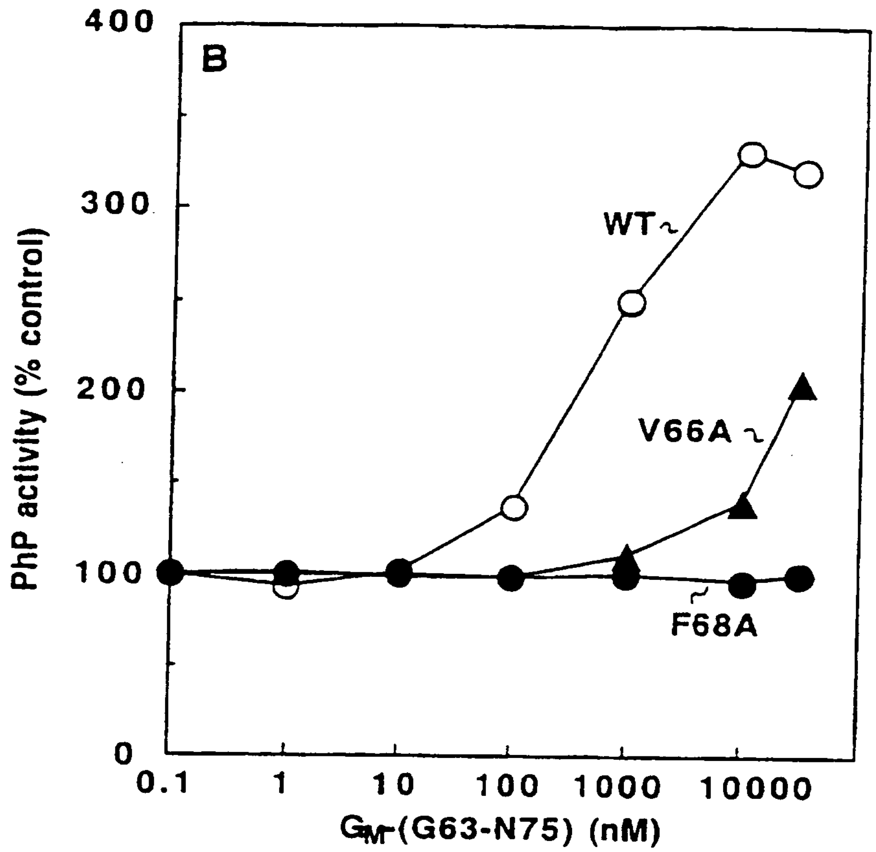

B
400
300
200
100
0
PhP activity (% control)
WT
V66A
F68A
0.1
1
10
100
1000
10000
G_M-(G63-N75) (nM)

Fig. 15B

Fig 16

Fig. 17

```
Rat     MKMADAKQKRNEQLKRWIGSETDLEPPVVKRQ KTKVKFDDGAVFLAACSS   50
Ch      MKMADAKQKRNEQLKRWIGSETDLEPPVVKRK KTKVKFDDGAVFLAACSS   50
Rat     GDTDEVLKLLERGADINYANVDGLTALHQACI DDNVDMVKFLVENGANIN  100
Ch      GDTEEVLRLLERGADINYANVDGLTALHQACI DDNVDMVKFLVENGANIN  100
Rat     QPDNEGWIPLHAAASCGYLDIAEFLIGQGAHV GAVNSEGDTPLDIAEEEA  150
Ch      QPDNEGWIPLHAAASCGYLDIAEYLISQGAHV GAVNSEGDTPLDIAEEEA  150
Rat     MEELLQNEVNRQGVDIEAARKEEERIMLRDAR QWLNSGHISDVRHAKSGG  200
Ch      MEELLQNEVNRQGVDIEAARKEEERIMLRDAR QWLNSGHINDVRHAKSGG  200
Rat     TALHVAAAKGYTEVLKLLIQAGYDVNIKDYDG WTPLHAAAHWGKEEACRI  250
Ch      TALHVAAAKGYTEVLKLLIQARYDVNIKDYDG WTPLHAAAHWGKEEACRI  250
Rat     LVDNLCDMETVNKVGQTAFDVADEDILGYLEE LQKKQNLLHSEKRDKKSP  300
Ch      LVENLCDMEAVNKVGQTAFDVADEDILGYLEE LQKKQNLLHSEKREKKSP  300
Rat     LIESTANMENNQPQKTFKNKETLIIEPEKNAS RIESLEQEKADEEEEGKK  350
Ch      LIESTANLDNNQTQKTFKNKETLIMEQEKNAS SIESLEHEKADEEEEGKK  350
Rat     DESSCSSEEDEEDDSESEAETDKTKPMASVTN ASTASTQAAPAAVTTPTL  400
Ch      DESSCSSEEEEDDDSESEAETDKAKTLA...N ANTTSTQ..SASMTAPSV  395
Rat     SSNQGTPTSPVKKFPTSTTKISPKEEERKDES PASWRLGLRKTGSYGALA  450
Ch      AGGQGTPTSPLKKFPTSTTKVSPKEEERKDES PASWRLGLRKTGSYGALA  445
Rat     EITASKEAQKEKDTAGVIRSASSPRLSSSLDN KEKEKDNKGTRLAYVAPT  500
Ch      EITASKEAQKEKDSAGVIRSASSPRLSSSLDN KEKEKDGKGTRLAYVAPT  495
Rat     IPRRLGSTSDIEEKENRES..SNLRTSSSYTR RKWEDDLKKNSSINEGST  548
Ch      IPRRLASTSDIDEKENRDSSASSIRSGSSYAR RKWEEDVKKN.SLNEGPT  544
Rat     .....YHRSCSFGRRQDDLISCSVPSTTSTPT VTSAAGLQKSFLSSTSTT  552/593
Ch      SLNTSYQRSGSFGRRQDDLVSSNVPSTAS..T VTSSAGLQKTLPASANTT  592
Rat     AKTPPGSSPAGTQSST SNRLWAEDSTEKEKDS APTAATILVAPTVVSAAA  587/643
Ch      TKSTTGSTSAGVQSST SNRLWAEDSTEKEKDS VPTAVTVPVAPSVVHAAA  642
Rat     SSTTALTTTTAGTLSS TSEVRERRRSYLTPVR DEESESQRKARSRQARQS  637/693
Ch      .TTTAMTTATSGTVSS TSEVRERRRSYLTPVR DEESESQRKARSRQARQS  691
Rat     RRSTQGVTLTDLQEAE KTIGRSRSTRTREQEN EEKDKEEKEKQDKEKQEE  687/743
Ch      RRSTQGVTLTDLQEAE KTIGRSRSTRTREQEN EEKEKEEKEKQDKEKQEE  741
Rat     KKESEVSREDEYKQKY SRTYDETYARYRPVST SSSSTPSSSSLSTLGSSL  737/793
Ch      KKESE.TKDDDYRQRY SRTVEEPYHRYRPTST .STSTSSTSSLSTSTSSL  789
Rat     YASSQLNRPNSLVGIT SAYSRGLTKDNEREGE KKEEEKEGEDKSQPKSIR  787/843
Ch      SSSSQLNRPNSLIGIT SAYSRSGTKESEREGG KKEEEKE.EDKSQPKSIR  838
Rat     ERRRPREKRRSTGVSFWTQDSDENEQERQSDT EDGSSKRDTQTDSVSRYD  837/893
Ch      ERRRPREKRRSTGVSFWTQDSDENEQEHQSDS EEGTNKKETQSDSLSRYD  888
Rat     ..SSSTSSSDRYDSLLGRSASYSYLEERKPYG SRLEKDDSTDFKKLYEQI  885/941
Ch      TGSLSVSSGDRYDSAQGRSGSQSYLEDRKPYC SRLEKEDSTDFKKLYEQI  938
Rat1/3                                                  ERRA  935/991
Rat2    LAENEKLKAQLHDTNMELTDLKLQLEKATQRQ ERFADRSLLEMEKRVTGK  935
Ch      LAENEKLKAQLHDTHMELTDLKLQLEKTTQRQ ERFADRSLLEMEKRVSGK  988
Rat1/3  LERRISEMEEELKMLPDLKADNQRLKDENGAL IRVISKLSK            976/1032
Rat2    SQYLLGGTKSSRKKNI                                      951
Ch      SQYLLGGKKSSRKKDI                                      1004
```

RECTIFIED SHEET (RULE 91)
ISA/EP

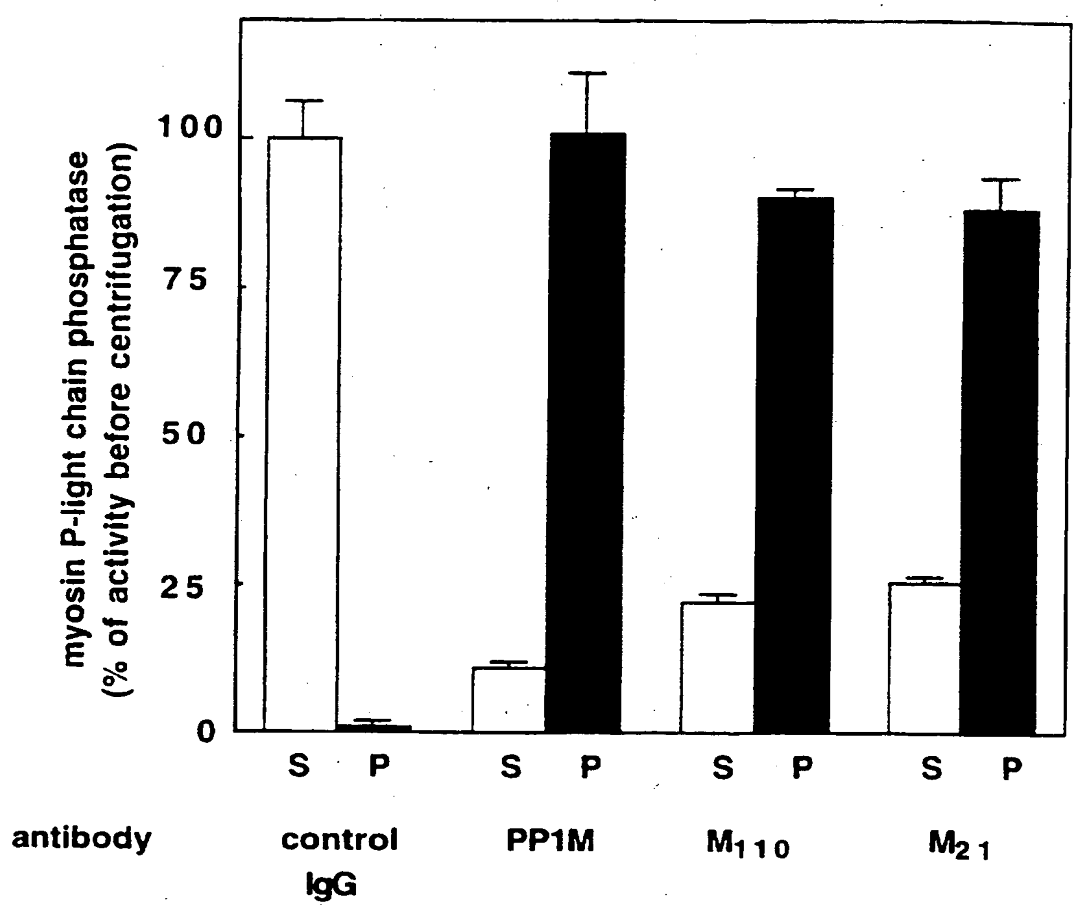

myosin P-light chain phosphatase
(% of activity before centrifugation)
100
75
50
25
0
S
P
S
P
S
P
S
P
antibody
control
IgG
PP1M
M110
M21

Fig 18A

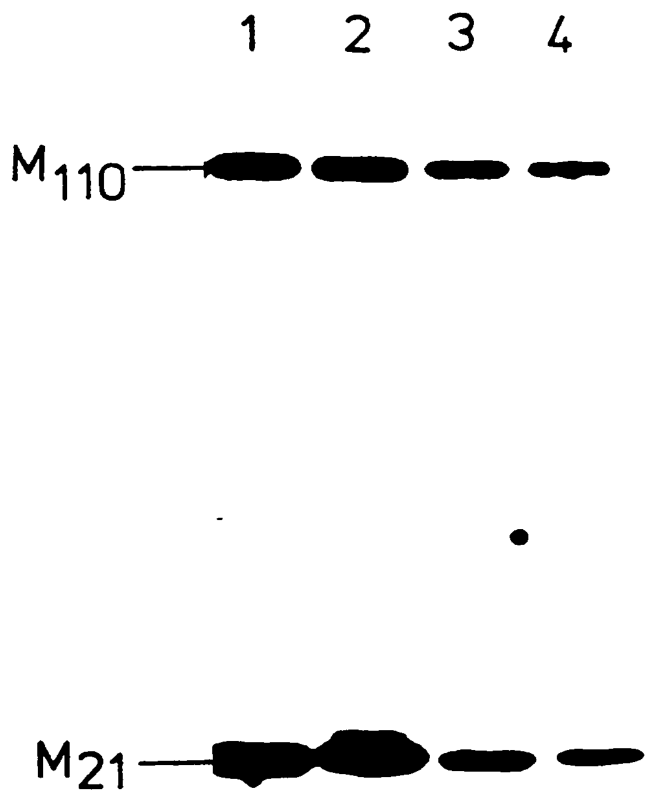


Fig 18B

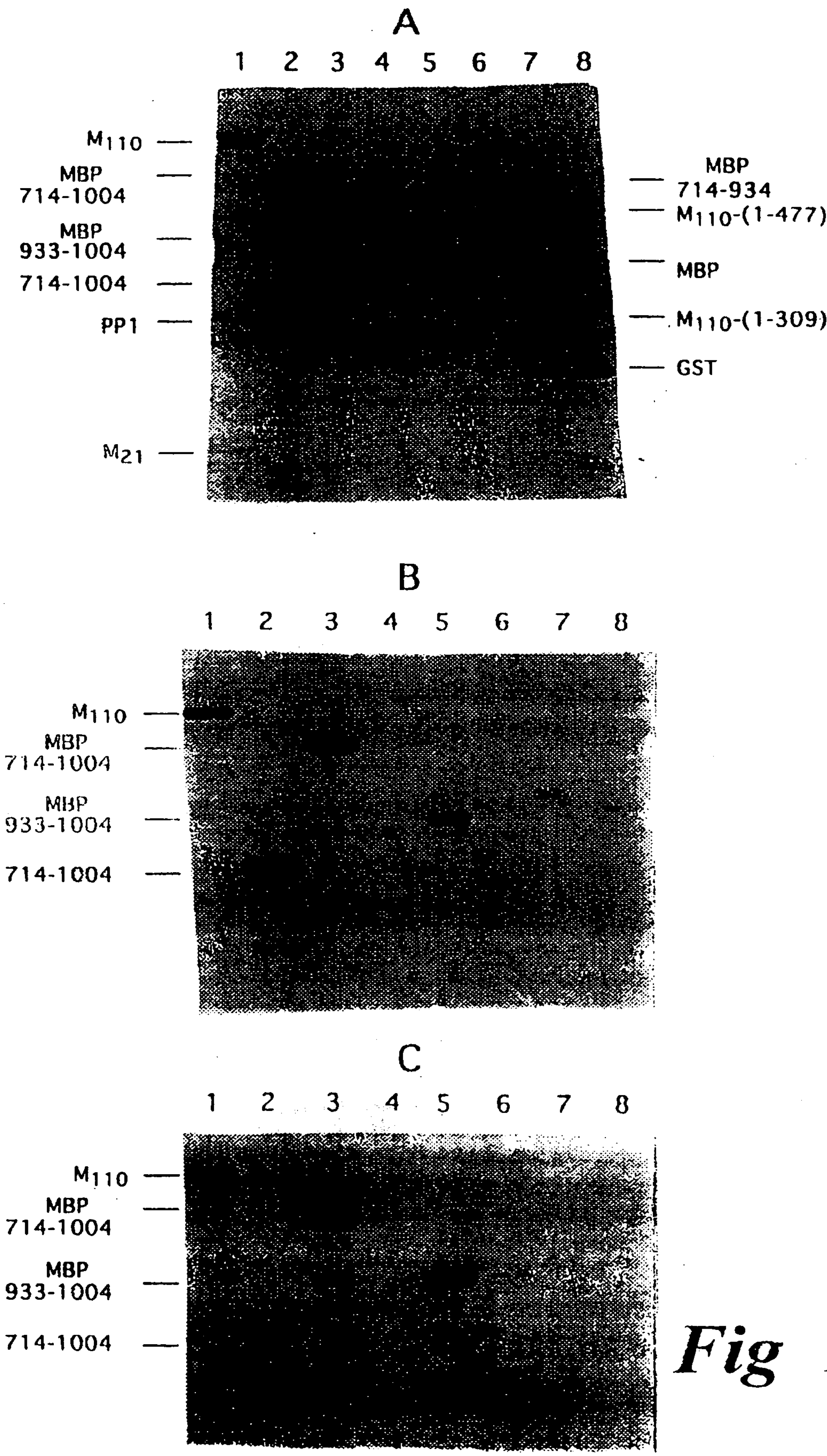

A
1 2 3 4 5 6 7 8
M110
MBP 714-1004
MBP 933-1004
714-1004
PP1
M21
MBP 714-934
M110-(1-477)
MBP
M110-(1-309)
GST
B
1 2 3 4 5 6 7 8
M110
MBP 714-1004
MBP 933-1004
714-1004
C
1 2 3 4 5 6 7 8
M110
MBP 714-1004
MBP 933-1004
714-1004

Fig 19

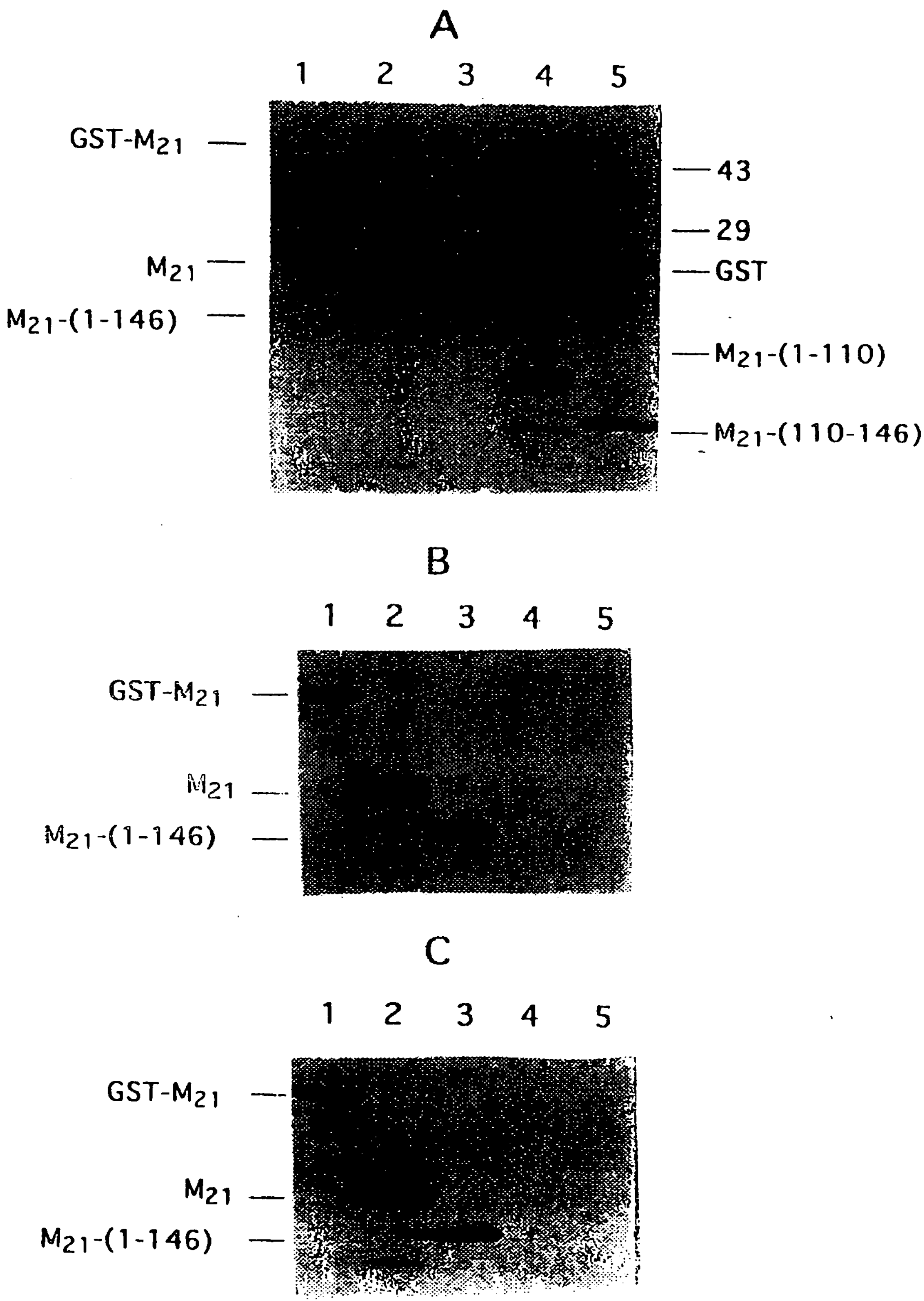

A
1 2 3 4 5
GST-M_{21}
M_{21}
M_{21}-(1-146)
43
29
GST
M_{21}-(1-110)
M_{21}-(110-146)
B
1 2 3 4 5
GST-M_{21}
M_{21}
M_{21}-(1-146)
C
1 2 3 4 5
GST-M_{21}
M_{21}
M_{21}-(1-146)

Fig 20

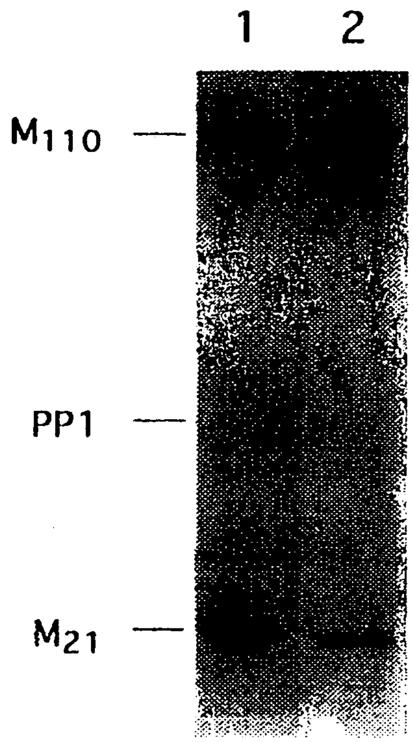


Fig. 21

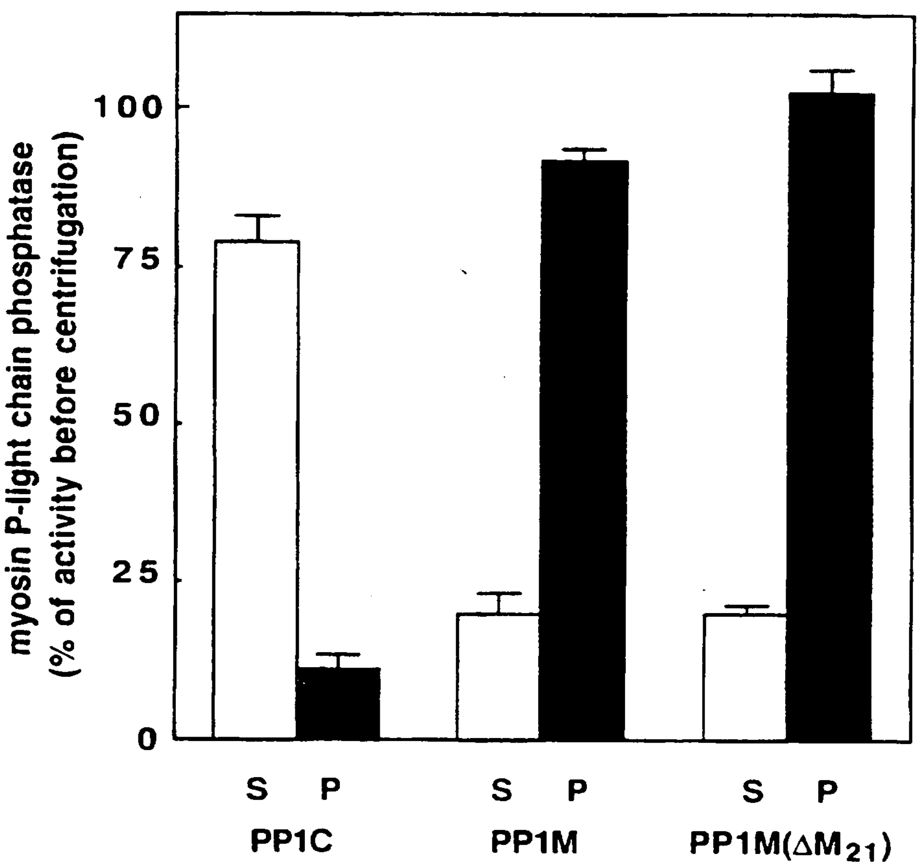
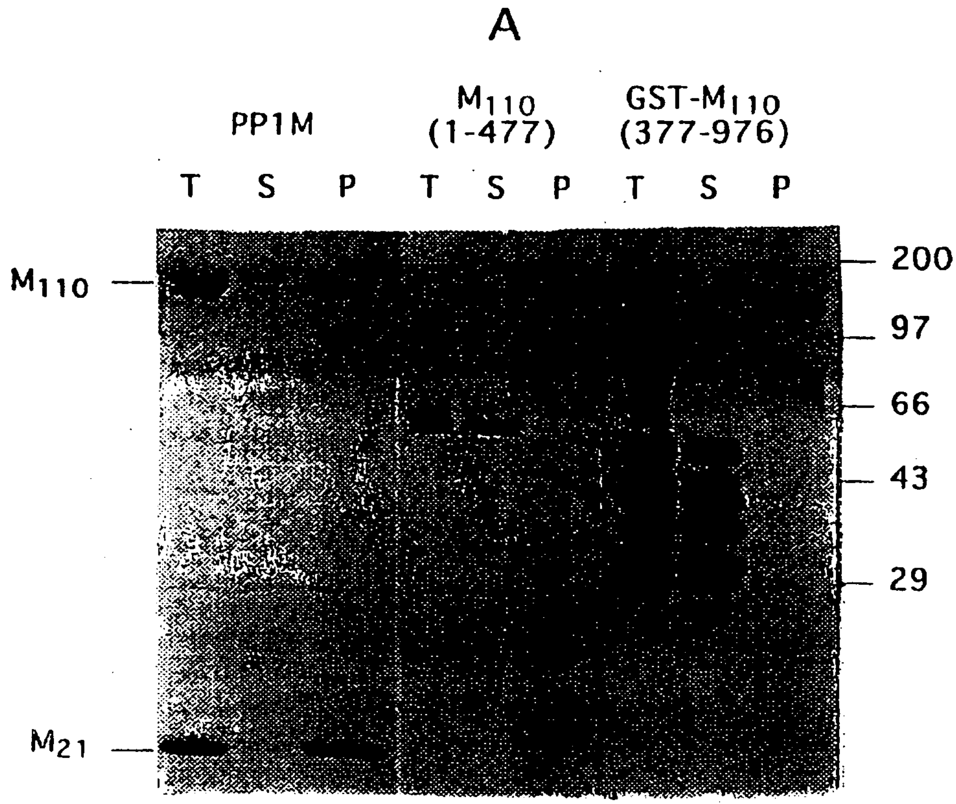

myosin P-light chain phosphatase
(% of activity before centrifugation)
100
75
50
25
0
S P
PP1C
S P
PP1M
S P
PP1M(ΔM21)

Fig 22


A
PP1M
M110 (1-477)
GST-M110 (377-976)
T S P T S P T S P
M110
M21
200
97
66
43
29

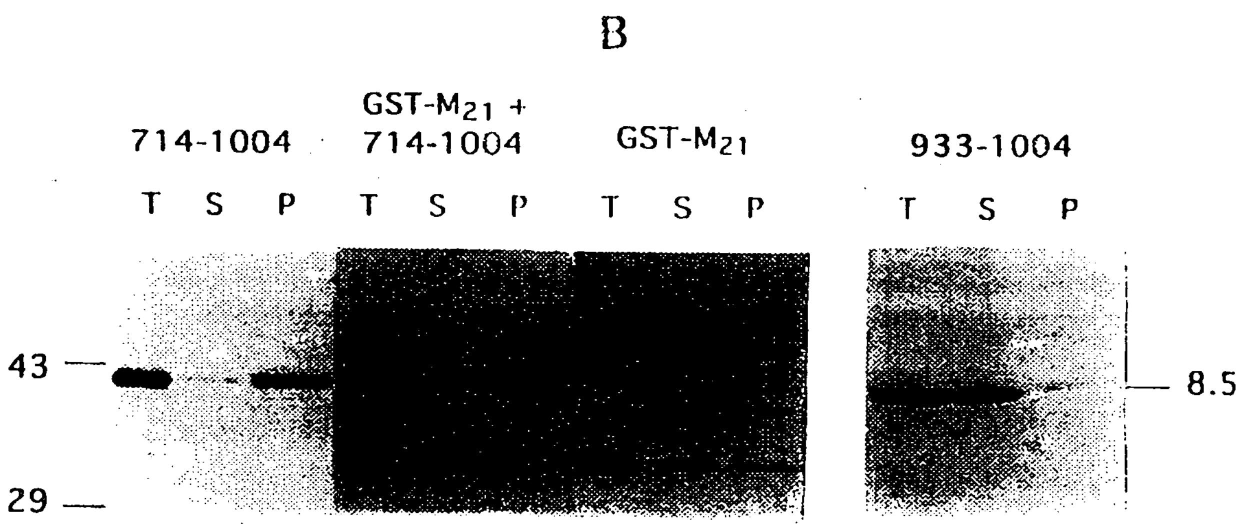

B
714-1004
GST-M21 + 714-1004
GST-M21
933-1004
T S P T S P T S P T S P
43
29
8.5

Fig 23

A

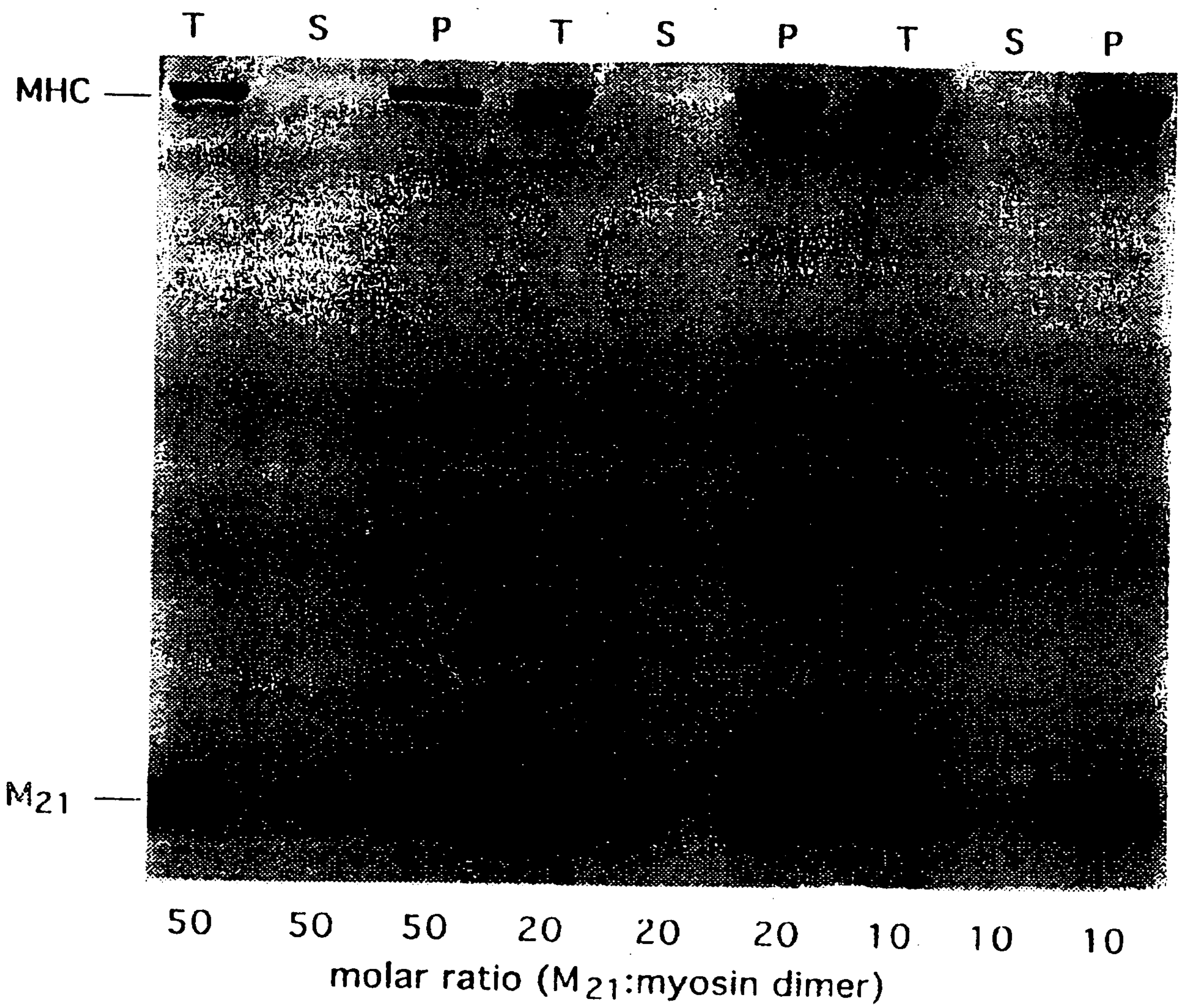

T S P T S P T S P
MHC
M21
50 50 50 20 20 20 10 10 10
molar ratio (M21:myosin dimer)

Fig. 24A

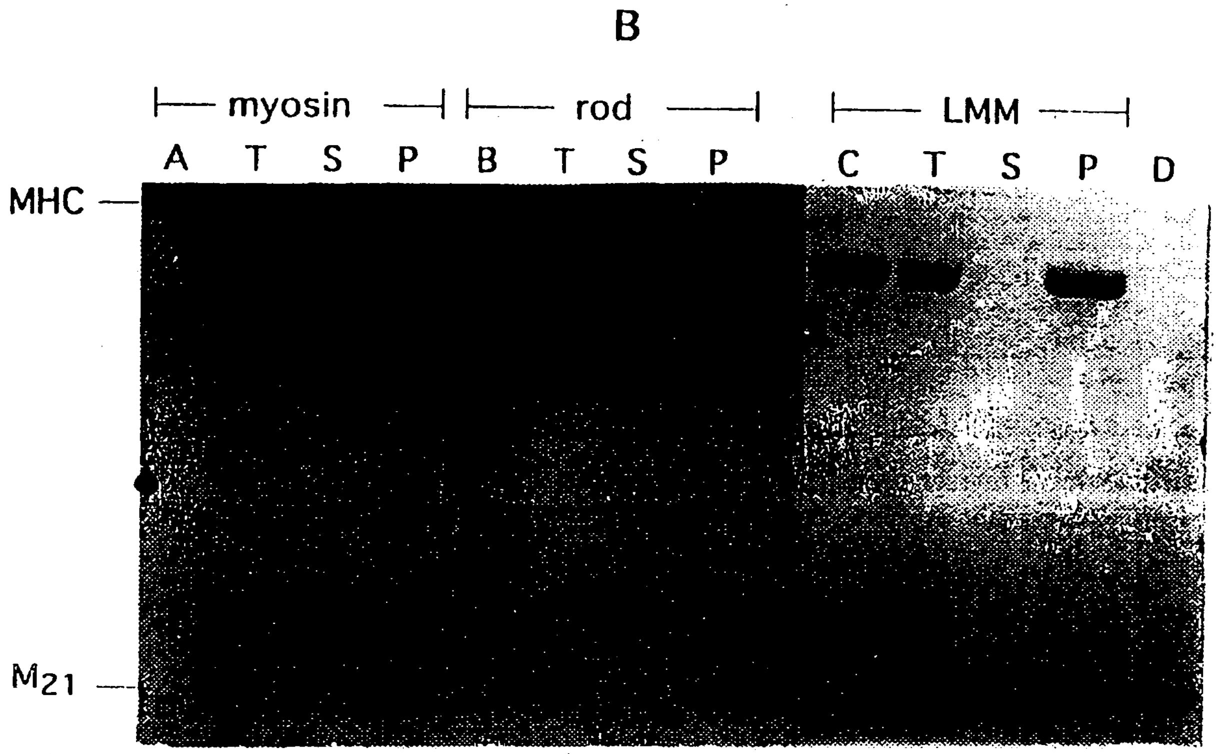


Fig. 24B

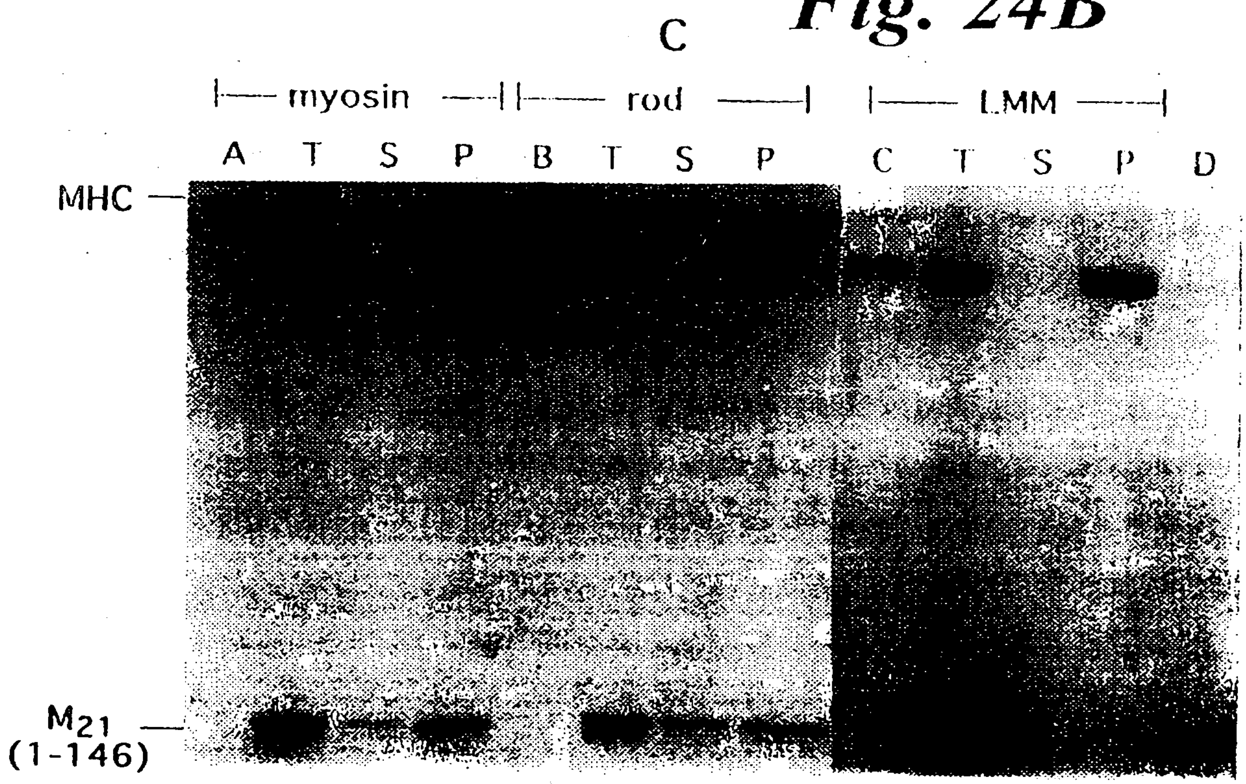


Fig 24C

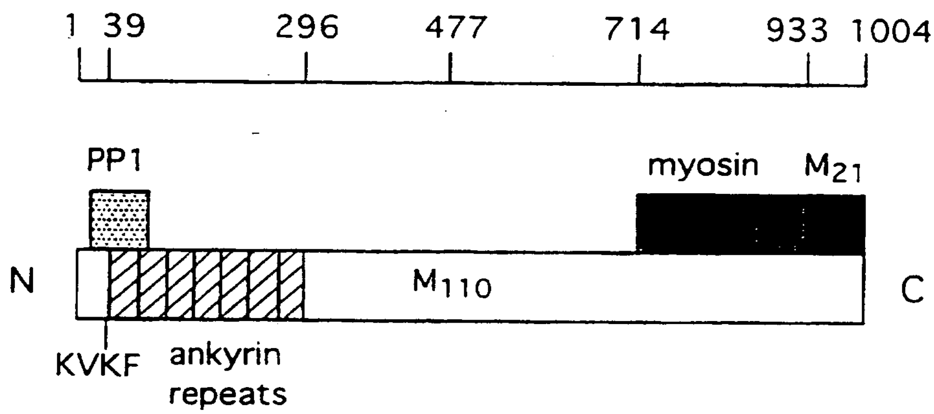

1
39
296
477
714
933
1004
PP1
myosin
M21
N
M110
C
KVKF
ankyrin
repeats

Fig 25

INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 97/00898

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 G01N33/573 C12N9/12 C07K14/435

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 G01N C12N C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	TRENDS IN BIOCHEMICAL SCIENCE, vol. 18, 1 May 1993, OXFORD UK, pages 172-177, XP002037474 M.J. HUBBARD ET AL.: "On target with a new mechanism for the regulation of protein phosphorylation" cited in the application see the whole document ---	1-35
A	JOURNAL OF MOLECULAR BIOLOGY, vol. 254, 1995, NEW YORK NY USA, pages 942-959, XP002037475 M.P. EGLOFF ET AL.: "Crystal structure of the catalytic subinit of human protein phosphatase 1 and its complex with tungstate." see the whole document ---	1-35

-/--

[X] Further documents are listed in the continuation of box C.

[ ] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

2

Date of the actual completion of the international search	Date of mailing of the international search report
13 August 1997	21-08-1997

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Van Bohemen, C

INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 97/00898

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	CRITICAL REVIEWS IN BIOCHEMISTRY AND MOLECULAR BIOLOGY, vol. 27, no. 3, 1992, BOCA RATON FL USA, pages 227-281, XP002037649 M. BOLLEN ET AL.: "The structure and role and regulation of type 1 protein phosphatase." cited in the application see the whole document ---	1-35
T	EMBO JOURNAL, vol. 16, no. 8, 1997, HEIDELBERG FRG, pages 1876-1887, XP002037247 M.P. EGLOFF ET AL.: "Structural basis for the recognition of regulatory subunits by the catalytic subunit of protein phosphatase 1." see page 1876, column 2, line 10 - line 49 -----	1-35

2

Form PCT/ISA/210 (continuation of second sheet) (July 1992)